

RESEARCH INSTITUTE, NEW DELHI

TROPICAL DISEASES BULLETIN

ISSUED UNDER THE DIREC-
TION OF THE HONORARY
MANAGING COMMITTEE.

VOL. 32. (Nos. 1-12.)
JANUARY—DECEMBER, 1935.

London :
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, W.C.1.

1935.

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ERRATA.

Vol. 32, No. 4, p. 246, BEQUAERT's summary, line 3 of title, for Blandfordia read Blanfordia, and for H. A. PILSBURY read H. A. PILSBRY. Also in text of summary read Blanfordia for Blandfordia throughout.

Regarding the summary of the article by MATHIS, LAIGRET & DURIEUX (pages 284-285), the authors have written saying that the statement regarding the occurrence of yellow fever after vaccination has been misinterpreted ; consequently the last 3 lines of the abstract should be deleted.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 1.

BERIBERI AND EPIDEMIC DROPSY.

AALSMEER (W. C.). Bijdrage tot de pathogenese der beri-beri. [**Contributions to the Pathogenesis of Beriberi. Parts I, II & III.**]—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. May 8. Vol. 74. No. 10. pp. 582-589; June 19. No. 13. pp. 776-782; July 3. No. 14. pp. 862-874. With 2 charts.

I. *Primary Beriberi due to B Avitaminosis*.—All the author's publications make special reference to the adrenalin test and its use as an indicator of the stage of the disease or the reality of cure and of the value of the therapeutic measures adopted. This test, it will be remembered, depends on the influence of adrenalin injections in active beriberi upon the diastolic blood pressure which is called, alternatively, the minimum tone pressure because it is the pressure registered by the sphygmometer at the moment when the auscultatory tone or bruit disappears with decompression of the brachial artery. Sometimes in beriberi an auscultatory murmur is already present before application of the recording instrument. In such cases, of course, the murmur cannot disappear with relaxation of pressure on the artery and the diastolic pressure is consequently registered as zero or nearly zero. No adrenalin test can be applied at all in such circumstances. But the essence of the test is that, when some diastolic pressure is registered, the administration of adrenalin in a hypodermic dose of 1 mgm. will, if observations are taken at five minute intervals, bring that pressure down to the zero point in an uncured case of beriberi. That is to say, the auscultatory murmur will persist even on complete relaxation of the pressure on the artery, as long as the patient is under the influence of adrenalin. This action of the adrenalin is due primarily to its effect on the heart itself but also to its dilating effect upon the peripheral blood vessels. The sum total of the different factors concerned is described under the word "gradient," expressing the fact that the rapidity of development of the fall in diastolic blood pressure and an unstable wave front are the most important factors concerned in this vascular syndrome.

By means of this test, then, Aalsmeer has been able to gauge the value of various dietaries, the interference of food substances themselves with vitamin absorption and the rôle which intestinal disturbance can play in the development of beriberi. Other influences, such as the psychic condition of the patient, may be determining factors in

preventing the disappearance of symptoms with the administration of vitamin B. This was the verdict in the case of prisoners on the island of Onrust, Java [this *Bulletin*, Vol. 31, p. 477].

There are other diseases than beriberi in which the weak tones of decompression take long to disappear or fail to disappear. Such diseases for example are exophthalmic goitre, aortic insufficiency and severe anaemias. The occurrence of this phenomenon in BASEDOW'S disease suggests that thyroid dysfunction or a pluriglandular syndrome may be at the root of some of the symptomatology of B-avitaminosis.

In certain cases the inoculation of adrenalin in a sufferer from beriberi failed to give rise to tone formation at low or zero diastolic pressures, a phenomenon attributable to decompensation of the left heart. The administration then of a preliminary injection of cardiazol was necessary to bring about stimulation of the heart, after which the adrenalin test became positive.

The methods referred to in this article have been tested out on patients. Such patients were in the first place given complete rest in bed and still kept on a vitamin-poor diet. The diastolic blood pressure, even if it were zero on admission, usually rose as the result of the simple rest in bed and this allowed of the application of the adrenalin test. A test case will illustrate the results obtained:—On admission the patient's diastolic pressure was zero. Even after five days' rest in bed it still remained zero. With the addition, however, of red rice to the vitamin-poor dietary for 8 days the pressure rose to 60. Then the adrenalin test was applied and the successive minimal diastolic pressures, at the usual five minute intervals, became 60, 50, 50, 50, 40, 0. That is to say zero pressure was again reached and the deduction could be made that the patient was not yet cured and his beriberi still remained active. After 15 days of a red rice dietary the improvement seen became a permanent one and the adrenalin test showed figures of 65, 65, 65, 65, 65, 65, or no diminution of diastolic pressure at all; repetition on the following day gave values 80, 75, 75, 70, 60, 70.

Besides red rice and Katjang idjoe a preparation of vitamin B, in tablet form or in ampoules containing liquid, may be equally effective for cure.

II. *Secondary Beriberi due to Disturbance of Intestinal Function.*—Although the administration of vitamin B should effect a cure in beriberi it is not the case that all or any vitamin-containing food will serve the purpose. This may be illustrated from actual cases and the test of the result should be the fall or absence of fall to zero of the diastolic pressure with the administration of adrenalin. A patient who was admitted to hospital and left for 7 days on vitamin-poor diet had a minimal diastolic pressure of 40. The adrenalin test brought this pressure down to zero. He was next placed for 6 days on red rice, dedek and tempe. Once more the adrenalin test brought the pressure to zero. And so it was with the addition of yeast. Purgation and 3 days of milk diet, with the idea of correcting gastro-intestinal disturbance, followed again by vitamin-poor food plus yeast gave a much improved adrenalin test as shown by the figures 65, 65, 40, 40, 40. This single example, out of the many given by the author, is intended to show that in spite of sufficient vitamin containing food avitaminosis can still remain, which may be due especially to disturbance of the intestinal functions (enterogenic beriberi). There are even cases in which none of the usual methods of feeding and not

even vitamin tablets themselves are successful. When patients then are treated by purgation or receive a milk diet for some days to promote normal intestinal functioning one may, as in the case of the patient mentioned, find that a return to the old vitamin-containing diet is effective. Again it may be found that withdrawal of red rice from the diet is promptly effective, presumably because the dietary contained an excess of carbohydrate. Place alongside these observations the fact that, when the enteral feeding of vitamin B fails the parenteral administration may give an immediate cure, and it is difficult to avoid the conclusion that disturbance of intestinal function of very peculiar type plays an important part in the development of a shortage of vitamin B.

III. *A. Delay in Recovery from Beriberi. B. Inactivity of Parenteral Vitamin B.*—In this communication it is shown that sometimes the parenteral administration of artificial vitamin B is unsuccessful whereas the same vitamin B given by the mouth brings about cure. This leads the author to the conclusion that artificial vitamin is not a full vitamin that it is, indeed, vitaminogen or provitamin, which is convertible in the intestine into the active product, vitamin B. If this conversion does not take place, whether in the intestine or by subcutaneous injection, the state of avitaminosis will persist. The hitherto observed cases of delayed recovery from beriberi are in all probability enterogenic forms of beriberi in the sense of SCHÜFFNER.

W. F. Harvey.

SOETJAHJO & GAN SING BIE. Over de werking van het antineuritische vitamine (B) van de I. G. Farbenindustrie A. G. bij een geval van beri-beri. [**On the Action of the Anti-neuritic Vitamin B in a Case of Beriberi.**—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. July 17. Vol. 74. No. 15. pp. 951-954.]

The adrenalin test of Aalsmeer has been made use of to gauge the value of the preparation of anti-neuritic vitamin used. If, moreover, a vitamin-poor diet first increases this effect of adrenalin and then the administration of vitamin B promptly causes it to diminish, it is considered legitimate to look on the test as a complete measure of the degree of beriberi affection.

The method of carrying out the test is as follows:—First of all the grade of beriberi is determined by application of the adrenalin test in conjunction with the pitressin test. Then the patient receives a vitamin-poor diet for 5 days. The adrenalin-pitressin test is next applied again. If now the symptoms appear changed for the worse, injections of the test vitamin are given (twice daily for 5 days), and the patient should then be enabled to remain on his vitamin-poor diet. The following case is illustrative:—"A patient with active beriberi, definite heart and vessel symptoms, pareses and oedema gave with rest in bed an increase in the minimal bruit-forming pressure and a slight increase of diuresis (but not more than 1,250 cc.)—an indication of relief of the strain upon the heart. When the vitamin-poor diet was begun there occurred first a lowering of the minimum bruit-pressure and then a rise, but it remained too low (40 mm.). The pulse remained still above 100, the oedema was unchanged and the pitressin effect remained negative after these 5 days of vitamin-poor diet, which is the testing indication that the beriberi had changed for the worse. The injections now given furnished the following result: (1) The diuresis was increased (2 litres) so that after the

injections were stopped the oedema diminished. (2) The pulse rate fell from over 100 to 76. (3) The minimal bruit-pressure increased from 40 to 60 mm. (4) The adrenalin reaction became negative. (5) Motor and sensory disturbances, although diminished, were still present

Thus it was shown that after subcutaneous injection recovery from the state of avitaminosis was rapid. The continued presence of neurological symptoms offers no contradiction, as they are no measure of the degree of deficiency in vitamin B (secondary degeneration). . . . It seems desirable therefore that the name anti-beriberi vitamin should be substituted for anti-neuritic vitamin." W. F. Harvey.

RIESMAN (David) & DAVIDSON (Harold S.). Beriberi following Drastic Voluntary Dietary Restriction—*Jl. Amer. Med. Assoc.* 1934. June 16. Vol. 102. No. 24. pp. 2000-2003. [11 refs.]

Two cases are described in which beriberi developed following the voluntary consumption of a deficient diet.

Particulars of the two cases are as follows:—

Case 1.—The patient, a white male aged 76, had for many years suffered from stomach trouble, with the result that he gradually eliminated different articles of food from his diet. About one and a half years before admission to hospital he was so ill that he gave up all food except milk, of which he took about three quarts a day. This caused diarrhoea, so that he was forced to reduce the milk intake by half. Progressive weakness set in, and his legs began to swell. On examination the man was found to be emaciated, pale and mentally confused. The hands, face and legs were oedematous, the calf muscles were extremely tender and the heart was enlarged to the right. The legs and buttocks also presented large ecchymotic spots. A diagnosis of beriberi was made. Two blood transfusions, of 250 cc each on successive days, were given, and, through a stomach tube, large amounts of vitamin B extract, orange juice, beef juice, egg, tomato juice and cod liver oil were administered, together with adequate doses of iron and ammonium citrate. After a few days the patient removed the tube saying that he could feed himself. He then developed a ravenous appetite and began to consume a normal diet supplemented with vitamin B extract and iron. Within two weeks the oedema subsided, and a month later he was able to walk about feeling cheerful and better than he had done for years.

Case 2.—A young woman, much over weight, tried to reduce her adiposity by living upon a meagre and monotonous diet. After a few weeks dyspnoea, palpitation and oedema of the legs appeared. No primary cardiac trouble was found, and beriberi was diagnosed. The return to a sensible diet alone resulted in prompt recovery.

The authors describe other similar cases collected from the literature, and they are of the opinion that "as long as fashion decrees the sylphlike figure, sporadic cases of beriberi are likely to occur." A. D. Bigland.

VAN VEEN (A. G.). Over het nut van niet gewasschen, weinig geslepen rijst als dagelijksch voedsel. [*The Use of a Ration of Unwashed Slightly Polished Rice.*—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. May 22. Vol. 74. No. 11. pp. 672-680. Full German summary.

This is a continuation of work already summarized in the *Bulletin*. A series of experiments is described dealing with the vitamin B₁ loss

sustained in the preparation of much larger quantities of rice, such as are used in the army, prisons and large plantations.

It was again determined that washing of rice of whatever degree of milling is very detrimental to its vitamin content, as proved by experiments with birds. On the other hand, steaming is very much less harmful in this respect, and also has the advantage of saving water and labour. Local objection (in Java) to unpolished or slightly polished rice, is chiefly on account of its red colour and not its taste; hence it is recommended that "silverskin" rice or other pale varieties be used, and that the washing of the product be omitted as far as possible. It is found by experience in prisons, plantations, etc., in Java that the custom of adding large amounts of vegetables as accessories to a polished rice diet is not acceptable to the native taste, especially when the consumption of large amounts of cooking water is also insisted upon.

A. D. B.

VAN VEEN (A. G.) & KOKS (M. T.) Over den invloed van het Claytoneeren op het B₁-vitamine-gehalte van rijst. [**The Effect of Clayton Disinfection on the B₁-Vitamin of Rice.**]*—Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Apr. 10. Vol. 74. No. 8. pp. 482-485.

In order that the experiments might be as natural as possible the samples of rice were taken from the holds of ships which had been Claytonized. The B₁-content was expressed in International Standard Units. In the first trials sacks of about 2-kilogram content were used and then sacks of larger size. Claytonization does affect the content of rice in vitamin B, and this reduction is greater the more polished and the moister the rice is. In sacks of some-kilogram size the B₁ vitamin of dry gabah rice is definitely diminished, that of dry silver-cuticle rice by more than one-third and that of half polished rice by about one-half. With larger sacks the effect is not so marked, due probably to non-penetration of the sulphur dioxide gas. Pure vitamin is practically not affected by a dilute solution of SO₂ at pH 3 to 7 and only slowly by concentrated solutions. The concentration of the B₁ vitamin in the samples used was estimated by trial upon rice birds.

W. F. Harvey.

SHIN (Hitsuko). **Basic Studies on Beri-Beri in Pregnancy and the Puerperium and also in Early Infancy.***—Trans. Soc. Path. Japon.* 1933. Vol. 23. pp. 295-306.

An account is given of experiments on rabbits showing the vitamin B content of the various organs under normal conditions and during pregnancy and the puerperium.

The vitamin content in the various organs of unmated rabbits was first studied. The liver and spleen give the highest figures, while progressively decreasing amounts were found in the kidney, lung and brain (equal), cardiac muscle, blood and voluntary muscles. The mammary glands contain none at all. During pregnancy the vitamin B content markedly decreases, especially in the liver, lung and brain. This is due not to excessive excretion from the kidney, where there is apparently an increased store, but to the increasing consumption of the vitamin by the growing embryo. An even greater fall in vitamin B content is found during the puerperium, but the kidney

still contains more than normal. The mammary glands during pregnancy and the puerperium contain an increased supply of vitamin. The above findings point to the liability of beriberi occurring in human subjects during this physiological state, especially if the vitamin B content of the diet is lessened.

A further series of experiments, this time using vitamin B-deficient diets, was carried out. It was found that feeding rabbits on such diets considerably reduced the vitamin B content of all organs and secretions, and the effect was especially marked during pregnancy and the puerperium. The liver was depleted more rapidly than the other organs. This is a most important finding since the liver is known to be a storage organ supplying vitamin B to the other tissues. It seems, therefore, that such diets during pregnancy and the puerperium must render the individual more than ordinarily liable to contract beriberi. On such vitamin B-deficient diets not only does the embryo suffer, but the vitamin content of the mother's mammary glands is decreased to one-fifth of that of a normally fed mother, and the suckling may easily contract beriberi. It was also found that such diets bring about important changes in the distribution of vitamin B throughout the body.

A third set of experiments showed that if the diet of the mother is lacking in vitamin B, even for a few days, the vitamin content of the embryo and of the mother is decreased. The same was found to be true of the mammary glands and the milk derived therefrom. Thus an infant may develop beriberi before the inadequately nourished mother shows any symptoms of the disease. A. D. B.

JOURNAL OF THE INDIAN MEDICAL ASSOCIATION. 1934. Sept.
Vol. 4. No. 1. pp. 12-13. **Epidemic Dropsy.**

Calcutta is again experiencing an outbreak of epidemic dropsy, and the present paper is in the form of an editorial dealing with the subject in general.

Among the epidemiological data are the following :—

The Northern part of the city is the more affected as it was in the epidemics of 1926 and 1932. Previous epidemics have been recorded in 1877, 1878, 1901, 1909, 1919, 1926, 1927, 1930, 1931 and 1932. "The morbidity is highest amongst the Bengali Hindus, moderate amongst the Mahomedans and least amongst the Marwaris. Europeans escape altogether." Some observers hold that the disease is due to the ingestion of toxins produced in badly stored rice by some spore-bearing bacillus, but in some outbreaks (as in Fiji) damaged rice cannot be held responsible. The taking of mustard oil is regarded by others as an important etiological factor. The following reasons are given in favour of the view that the disease is probably not a primary intoxication but an infection :—

- " (1) Seasonal incidence in July when long continued rains and humidity are present.
- " (2) Widespread epidemicity.
- " (3) Greater incidence amongst people living in riverside places, suggesting the possibility of a water-borne infection.
- " (4) Occasional incidence of the disease amongst persons who come in contact with a patient of epidemic dropsy where dietetic and environmental factors have been definitely eliminated.

- "(5) The frequent spread of the disease from towns to the villages.
"(6) Recurrent and chronic course of the disease as is shown by the persistence or re-appearance of oedema of the legs, of gastro-intestinal and cardiac disturbances."

It is suggested that further research should be directed towards the bacteriological study of the intestinal flora of sufferers together with immunity reactions against any suspected organism isolated. Attempts should also be made to reproduce the disease in suitable experimental animals.

A. D. B.

PURCELL (F. M.). **Beri-Beri or Epidemic Dropsy.**—*West African Med. J.* 1934. Apr. Vol. 7. No. 4. pp. 143-145.

A case of general anasarca in an African child is described. A diagnosis of epidemic dropsy was made. The child had lived exclusively upon cassava, and details of the preparation of this tuber are given.

Beriberi is uncommon in the Gold Coast, only 16 cases being reported in 1930 and a smaller number in the following year. Rice is the staple food of the Kroos alone, but the disease apparently is not confined to this tribe. If vitamin deficiency were the sole cause of beriberi the disease should occur sometimes in epidemics since in any one tribe the staple food is constant. Such epidemics have not been observed in the Gold Coast, and it seems that none of the tribal diets is deficient in neuritis-preventing vitamin.

One case is described. The patient, an African child, was admitted to hospital having been sick for one week. He presented general anasarca, marked tachycardia with orthopnoea, enlarged heart with signs suggesting hydropericardium, mild fever and hepatic and splenic enlargement. The knee jerks were absent, but it is stated that subsequently no evidence of peripheral neuritis was discovered. The patient was successfully treated with heart tonics and magnesium sulphate. The author is of the opinion that this was a sporadic case of epidemic dropsy.

The child's diet consisted of cassava and apparently nothing else. In the Ada district the diet consists almost exclusively of this tuber, which is scraped and dried in the sun. While drying a black saprophytic fungus, *rhizopus*, grows upon it, and the natives think that this improves the food. Cassava is practically pure carbohydrate with very little protein and probably also deficient in vitamins. The physique of the Ada people is poor in consequence.

A. D. B.

MASSIAS (Charles). Présence de bacillus méésentériques dans une hémoculture au cours d'un épisode fébrile chez un ancien béribérique.—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Feb. Vol. 12. No. 2. pp. 173-174.

MÉHES (J.). Die Wirkung der Digitalisglykoside bei an Beriberi erkrankten Tauben.—*Arch. f. Experim. Path. u. Pharm.* 1934. Aug. 30. Vol. 176. No. 2/3. pp. 141-159. With 2 figs. [14 refs.]

— & PÉTER (F.). Die Wirkung des Digitoxins auf das Ekg der normalen und der an experimenteller Beriberi erkrankten Tauben.—*Arch. f. Experim. Path. u. Pharm.* 1934. Aug. 30. Vol. 176. No. 2/3. pp. 226-237. With 5 figs. [24 refs.]

SLEEPING SICKNESS.

DUKE (H. Lyndhurst). On the Protective Action of "Bayer 205" against the Trypanosomes of Man.—*Lancet*. 1934. June 23. pp. 1336-1338.

Details are given of a number of experiments devised with the object of ascertaining how long Bayer 205 would protect man against infection with *T. rhodesiense* and *T. gambiense*.

In his introductory remarks, Duke states that although prevention is better than cure, prophylaxis against the diseases of man by the use of drugs could claim little or no success before the appearance of "Bayer 205." For many years the medical profession has been debating about the value of quinine as a prophylactic in malaria. The work of the reviewer and MACFIE (1924) was, however, the first scientific warning that all might not be well with the time-honoured ritual, practised the world over by Europeans "east of Suez," of the 5-grain tablet taken each evening with the first "sundowner." A commission of the League of Nations has studied the question experimentally, and in the third general report of the Malaria Commission the conclusion is promulgated that "No drug which is known, taken in harmless doses, can be guaranteed to act as a true causal prophylactic."

A summary is given of the earlier observations of the prophylactic action of "Bayer 205" against infection in animals and man with various trypanosomes. Although the general inference to be drawn from this work is that "Bayer 205" has a definite prophylactic value, nevertheless the evidence so far accumulated is not entirely conclusive.

The author's experiments were commenced in connexion with an investigation on the effect of long residence in antelope of the trypanosomes of man. Volunteers were used for this work and those who became infected were treated with "Bayer 205" the moment trypanosomes were demonstrated in their peripheral blood. Three of these cases (A, B and C) were chosen as the starting point of the present research. Each of these men was infected with a strain of *T. rhodesiense* which had been for months in an antelope at the laboratory. All three became infected after an incubation period of 8 to 10 days, and each was treated with a series of 6 doses of 1 gm. of "Bayer 205," the doses being given at an interval of a few days.

At the Conference on Trypanosomiasis held last November at Entebbe, the examination of the prophylactic value of "Bayer 205" was allocated to the Uganda Institute. Three healthy native volunteers (cases I, M and Q) were selected, and each was given a single intravenous injection of 1 gm. of "Bayer 205"; and another treated volunteer (E) was added to the first list. In addition, 3 monkeys were also given a prophylactic dose of the drug varying from 0.158 gm. to 0.023 gm. per kilo.

At various intervals, after the administration of the drug, the volunteers and the monkeys were subjected to the bites of tsetse flies infected with different strains of *T. rhodesiense* and *T. gambiense*, respectively. Details are given in the table, which is reproduced (p. 9).

Those volunteers (A, B, C and E) who had been treated with 6 doses of "Bayer," after being infected for some 10 or 11 days with *T. rhodesiense*, resisted all attempts at re-infection with different strains of *T. rhodesiense* for at least 190 days. On the other hand, the

Litter size last inoculation of Beyer 205	Volunteers							Monkeys				Days after last inoculation of Beyer 205	Volunteers						
	A	B	C	E	I	M	Q	1225†	1227†	1229†	A		B	C	E	I	M	Q	
38	2g	103	1d	..	5b ³	..		
39	3a	104	2b ³	..	1b ³	..		
40	2a	1b ³	105	2b ³	..		
63	1b	1b ³	107	6b ³		
66	108	1b ³	..	1b ³		
67	1b ³	110	3b ³		
68	1c	111	4b ³		
69	1c	1b ³	..	113	fe	..		
70	1c	1b ³	..	133		
72	134	1b ³		
74	1c	1c	1d	136	1b ³		
75	2b ³	2b ³	142	2b ³		
76	145	2b ³		
77	1d	1d	1d	146	1c	**1g ³	..		
78	2b ³	2b ³	147		
79	1d	1d	149		
80	2b ³	2b ³	1b ³	1b ³	174	1d		
81	179		
82	180		
83	1d	1d	181	1b ³		
88	182	1b ³		
91	1b ¹	187	1c	2b ³		
92	3b ¹	190	2e		
95	2b ¹	208		
99	210		
100	..	1b ¹	212		

EXPLANATION.

The numerals in the columns show the number of gland-infected flies biting man on that date.

[illegible]

† Trypanosomes appeared in 1229's and 1229's blood 11, 9 and 8 days respectively after the first fly bite.

monkeys were found to be sensitive to infection with *T. rhodesiense* 67, 69 and 74 days respectively after treatment with a single dose of "Bayer." It is to be noted that each of these animals proved to be sensitive the first time it was examined.

Duke states that the results obtained with *T. gambiense* are particularly instructive. Volunteer M was bitten on the 113th day by a fly infected with *T. rhodesiense*, but he did not become infected. On the 145th day he was bitten by 2 flies infected with *T. gambiense* and 9 days later was found to be infected. From this, Duke concludes "The administration of a single dose of 'Bayer 205' had therefore protected this man against *T. rhodesiense* for at least 113 days, but by the 145th day he was no longer safe against *T. gambiense*." Turning to the 6-dose series of volunteers, it is seen that B was bitten by 7 flies infected with *T. gambiense* between the 208th and 212th days after the last dose of "Bayer"; 22 days later he was found to be infected. It thus appears that volunteer B, who was protected against *T. rhodesiense* for at least 180 days after the last administration of "Bayer 205," possesses no defence against *T. gambiense* on the 208th day. It has not yet been determined how long protection lasts against *T. gambiense* in man; the only other experiment performed with this trypanosome being that of volunteer C who resisted infection 38 days after his last dose of "Bayer 205."

In his conclusions Duke states that it is probable, though not yet proved, that the protection conferred by "Bayer 205" is greater against *T. rhodesiense* than against *T. gambiense*. He adds that at the present time, to be on the safe side, he considers that the prophylactic injection of 1 to 1.5 gm. of "Bayer 205" per adult should be repeated every 3 months while exposure to infection continues. He further considers that the natural sensitiveness of the mammal to the trypanosomes plays an important part in determining the duration of the protection conferred by "Bayer 205," the more susceptible monkey receiving less protection per dose per kilo. of body weight than the more resistant man.

W. Yorke.

DUKE (H. Lyndhurst). **On the Employment of Volunteers in Trypanosomiasis Research; and on the Element of Control in Experiments with Trypanosomes and Glossinae.**—*Parasitology*. 1934. Aug. Vol. 26. No. 3. pp. 315-324.

Two subjects are dealt with in this paper which, in the author's opinion, are of practical importance to those interested in research on trypanosomiasis; these are the employment of volunteers and the necessity for control in experiments on *Glossina*.

In discussions on the zoological status of *T. gambiense*, *T. brucei*, and *T. rhodesiense*, it is generally assumed that *T. brucei* cannot infect man, whereas the other two can. The true affinities of all these trypanosomes can, however, be revealed only by direct experiments on man himself, and until the last year or so the risks connected with such experiments precluded their employment on anything like an adequate scale. Recent advances in chemotherapy have removed the main obstacle to experiments on man, and it is now safe to use volunteers. CORSON was the first to test on himself a trypanosome known to have been at one time pathogenic to man [this *Bulletin*, Vol. 29, p. 634], and shortly afterwards FAIRBAIRN performed a similar experiment on himself.

The employment of native African volunteers began with certain investigations carried out at Entebbe two years ago. Duke states that

he thinks all will agree that it is in practice impossible to settle the unsolved problems of trypanosomiasis without the assistance of native Africans: the number required alone justifies this contention. Up to the present, in the investigations in Uganda into the antelope reservoir and the prophylactic results of "Bayer 205," 24 native volunteers have been employed. All these men fully understood the significance of their contract. So far 16 of them have become infected and there has been no untoward event in the subsequent career of any. The regular method of infection employed is the bite of a cyclically infected fly, or, in rare instances where this is impossible, the subcutaneous inoculation of its glands. In addition to the more obvious points to be considered with the use of volunteers, there is the theory recently advanced by CORSON that there may be a state of cryptic trypanosomiasis set up in man by strains of *T. rhodesiense* which have been exposed for long periods to the tissues of resistant animals such as antelope [this *Bulletin*, Vol. 29, p. 634]. After considering this matter in some detail, Duke comes to the conclusion that it is very unlikely that this hypothetical cryptic infection with *T. rhodesiense* ever occurs in man.

Dealing with the second subject, Duke states that in any prolonged investigation on African mammalian trypanosomes, especially where *Glossina* are used as agents of infection and ruminants as the vertebrate host, it is of the first importance to establish an efficient system of control against accidental infection with trypanosomes other than those which it is intended to investigate. During the last year or two the main subject of research at Entebbe has been the study of game animals, especially antelope, as a reservoir of the trypanosomes of man, and in such an inquiry supreme importance attaches to the question whether a given trypanosome is or is not pathogenic to man. To carry out this research clean antelope were collected at the Institute and some of them were set aside as controls. Some months ago, one of the control animals was found to be infected with a trypanosome indistinguishable from the *T. rhodesiense* carried by its experimentally infected companions.

In the antelope enclosure there lived freely together three adult bushbuck, 4 oribi, one adult and 2 young situtunga, 4 reedbuck, and a ntalaganya. Of these, one of the situtunga, a ntalaganya and a reedbuck were kept as controls. After some time it was discovered that the control reedbuck was infected.

Duke examines in great detail the possible ways in which this untoward event had occurred. For reasons given he is able to exclude the possibility of the control reedbuck being infected when it reached the laboratory, and similarly he excludes the possibility that the animal was infected with wild *Glossina palpalis* as he is satisfied that these flies never succeed in reaching the present laboratory. The explanation of the phenomenon seems to be the direct transmission of the trypanosomes ruminant to ruminant by *Stomoxys*. The three young reedbuck were observed to keep close together all through the day, thus facilitating the direct transference of trypanosomes from one to the other. Moreover, trypanosomes were common in their peripheral blood. *Stomoxys* were numerous in the animal enclosure and dissection of several hundreds caught in the antelope's stable revealed in the partially digested blood of the hind-gut of a single fly a few feebly-moving trypanosomes which had presumably been taken up from one of the antelope.

W. Y.

BRITISH EAST AFRICAN TERRITORIES, CONFERENCE OF GOVERNORS OF: Research Conferences. Conference on Tsetse and Trypanosomiasis (Animal and Human) Research. Held at Entebbe, 22nd to 25th November, 1933.—42 pp. 1934. Nairobi: Govt. Printer.

The Governor of Uganda in opening the Conference stated that this was the first of what he hoped will prove an exceedingly valuable series of conferences. The co-ordination of scientific research in East Africa is one of the duties which has been specially assigned to the Governors' Conference, and when they discussed the question last February they reached the unanimous conclusion that at the moment co-operation and co-ordination were not as complete as they might be. With the object of remedying this they had decided to call together representatives of the various East African Colonies of Kenya, Nyasaland, Tanganyika and Uganda. He also welcomed Dr. FONTANA, Chief of the Medical Service of the Province Orientale of the Belgian Congo.

The Agenda is divided into three sections:—

A. Items from the programme of Research suggested by the Second International Conference on sleeping sickness [this *Bulletin*, Vol. 26, p. 185]. These include—the question of natural immunity, spontaneous cure and acquired immunity of man, and natural immunity of the baboon and its relationship with serum-resistance; other reservoirs of *T. gambiense* than man and new means of diagnosis; the origin of *T. rhodesiense* and its relationship to *T. gambiense* and *T. brucei*; the transmission of acquired characters through *Glossina*; the evolution of the polymorphic trypanosomes in tsetse and the factors which influence it; pathological investigations in infected animals; biological studies of tsetses; the factor determining the infectivity of trypanosomes for tsetse; therapeutic researches, etc.

B. Items of research suggested by investigators in the East African Territories, e.g., bionomics of *T. uniforme* and *T. brucei*; cultivation of trypanosomes; the control of trypanosomiasis in man and animals by chemotherapy, by administrative methods, and by control of tsetse; diagnostic methods in trypanosomiasis; mechanical transmission of trypanosomes by vectors other than tsetse; the pathogenicity of various trypanosomes for different animals, etc.

C. The future of trypanosomiasis and tsetse fly research in East Africa.

At the general discussion which took place on the agenda, it was decided to arrange the program of research first, leaving the question of the future of trypanosomiasis and tsetse-fly research in East Africa to be dealt with later.

After much discussion a program of tsetse and trypanosomiasis research was agreed upon; this program is summarized in the table (p. 13).

The Conference then proceeded to the discussion of the future of trypanosomiasis and tsetse research in East Africa. After DUKE had outlined the position in regard to protozoological research and the financial difficulties of the Human Trypanosomiasis Institute, the Conference considered the advisability of preserving a Central Research Institute, and the opinion was expressed that the present was not a time at which a definite pronouncement on such a subject could be made. It was felt that, whether or no a Central Institute

could be established, other laboratories where local problems in connexion with trypanosomiasis could be investigated would still be essential. Finally the Conference :—

- " (1) considered that the present time was inopportune to give an opinion as to whether the Human Trypanosomiasis Institute should be continued as a permanency ;
- " (2) recommended that, if the Government of the Uganda Protectorate agreed, this Institute should be kept on for another year on its present footing and that the question should then be reconsidered ;
- " (3) having discussed the programmes of research in hand in the various laboratories and in the field, recorded its opinion that no overlapping of research was taking place in East Africa other than that which was necessary for the establishment of essential facts."

Summary of Program of Tsetse and Trypanosomiasis Research.

a = Human Trypanosomiasis Institute, Entebbe.	d = Trypanosoma Rhodesiense Laboratory, Tinde.
b = Veterinary Laboratory, Entebbe.	e = Medical Laboratory, Nairobi.
c = Veterinary Laboratory, Mpwapwa.	f = Medical Laboratory, Nyasaland

Item of Research	Where to be carried out
(a) Question of natural immunity, spontaneous cure and acquired immunity in man ...	a, c and d.
(b) Experiments on relatively resistant ruminants with strains of <i>T. rhodesiense</i> and <i>T. gambiense</i> obtained over as wide an area as possible ...	a, c and d.
(c) Existence of other reservoirs of <i>T. gambiense</i> than man ...	a.
(d) Retention of acquired characteristics by trypanosomes during cyclic evolution in body of tsetse ...	a (<i>T. gambiense</i>). c (<i>T. congolense</i> and <i>T. vivax</i>). d (<i>T. rhodesiense</i>).
(e) Evolution of different trypanosomes in body of tsetse and other biting flies and relationship to environment (climate, etc.) of cyclic transmissibility and pathogenicity ...	a, b, c, and f.
(f) Biological studies of tsetse-flies in <i>T. rhodesiense</i> , <i>T. gambiense</i> and <i>T. brucei</i> areas ...	Work now being carried on in various territories to be continued.
(g) Study of food supply of tsetse as determined by biological study of stomach contents of fly ...	e.*
(h) Investigation of the prophylactic value of Bayer 205 ...	a.†
(i) Further investigation of identity of <i>T. uniforme</i> ...	a and b.‡
(j) Investigation of bionomics of <i>T. brucei</i> ...	b.
(k) Cultivation of <i>T. congolense</i> and <i>T. vivax</i> on artificial media ...	b.
(l) Control of tsetse-fly ...	Work now in hand or projected in all territories to be continued or put in hand.
(m) Trypanosomiasis of pigs ...	b and c.§

* Mr. Swynnerton prepared to assist in supply of sera from game animals when opportunity offered.

† A large-scale field experiment to be conducted in Tanganyika should the laboratory experiments indicate the necessity therefor.

‡ Every endeavour to be made to furnish a strain to Mr. Hornby.

§ Material acquired in any territory to be transmitted to either of these laboratories.

SWYNNERTON then explained the present position and the amount of collaboration which was already in existence as regards tsetse-fly research in East Africa. The Conference after some discussion :—

- " (1) recorded its appreciation of the great practical importance of the work of the Tanganyika Tsetse Research Department to all three territories as regards the control of both animal and human trypanosomiasis (*vide* Appendix III) ;
- " (2) recorded its conviction of the need, not only for this work, but also for every facility being given by the respective Governments to continue and extend the present opportunity for personal co-operation and collaboration without regard to inter-territorial boundaries."

A discussion took place on the facilities which existed for the communication of results of the trypanosomiasis research which is being carried on in the various laboratories in the Colonial Empire. DUKE and CORSON informed the Conference of the very valuable help they had received from the "Tropical Diseases Bureau." The Conference, after discussion :—

- " (1) recorded its opinion that further facilities for the distribution of published and unpublished reports should be given, and recommended that some central body in England should be approached with a view to its undertaking the distribution of reprints, etc., to workers who might be interested ;
- " (2) recognized that this would involve the provision of a greater number of reprints, and recommended that the cost of such should be borne by the Government concerned."

The report closes with a memorandum by MACLEAN on the control of trypanosomiasis in man and animals by chemotherapy and administrative measures ; and with a memorandum by SWYNNERTON giving an account of the work which had been carried out in East Africa either by the Tsetse Research Department in Tanganyika or by members of the Medical and Veterinary Departments in other territories in collaboration.

W. Y.

LEDENTU (G.). La lutte contre la maladie du sommeil au Cameroun. [**Campaign against Sleeping Sickness in Cameroon.**]*—Ann. Inst. Pasteur.* 1934. Aug. Vol. 53. No. 2. pp. 174-220. With 8 diagrams.

This paper describes the work of the sleeping sickness organization in Cameroons since 1930. In a recent paper JAMOT has summarized the work of the mission between 1924 and 1930 [*this Bulletin*, Vol. 29, p. 633].

In 1931 the sleeping sickness prophylaxis service was dissolved and the whole organization changed, owing to the acute economic crisis. From 36 European officers and 400 native assistants it became necessary to reduce the service to a minimum compatible with safety. The new organization, which still remained centred in Ayoos, the main epidemic focus, consisted of 5 teams for diagnosis, each composed of a doctor and 20 assistants, and more than a dozen teams for treatment, each composed of a European sanitary officer and 3 hospital attendants. The general organization which had proved so satisfactory in the past was thus maintained but modified so as to meet the financial needs of the time. In 1934 it was found possible to reinforce the service to some extent.

The very lengthy report which follows takes the same general form as that of JAMOT, 1932. A detailed account is given of the progress of the disease in the various subdivisions of the epidemic zones, in which the initial morbidity was everywhere over 15 per cent. ; in the endemo-epidemic zones, in which the infection rate was in some places over and in other places less than 15 per cent. ; and finally in the endemic zones, in which the infection was everywhere less than 15 per cent. [Those interested must consult this part of the paper in the original.]

The general impressions produced by this summary appear to be :—

1. In the zones of feeble endemicity the disease has nowhere gained ground and in places it has definitely retrogressed.

2. In the endemo-epidemic zones the results have been considerable. The vast focus in the north constituted by the subdivisions of Doumé and Nanga-Eboko has been reduced to one of feeble endemicity. The two western foci of Manguissas and Etons appear to be extinct ; that of Bafia is reduced to the Yambassa tribe, but here it offers a stubborn resistance. The southern focus of Sangmélina has almost disappeared.

3. In the epidemic zones the focus of Bertoua is extinct, as is almost that of Batouri. The same cannot be said, however, of the foci of Haut Nyong and of the upper reaches of the Dja ; and there is some revival of activity among the Omengs, the Makas and the Yébékolos of Akonolinga.

The broad facts emerging from this survey are that the disease has undergone rapid retrogression, sometimes spontaneously, in most of the peripheral zones of extension, but that there is some recrudescence in the old foci. In the old foci of Nyong and of Dja the infection is proving resistant and in certain places is even increasing, but the index of peripheral infection is, however, not comparable with that observed in 1926–1928, when it was 35 to 45 per cent. To-day such a figure as 5 per cent. is exceptional.

It is difficult to understand why trypanosomiasis in certain zones readily yields to treatment, whilst in others it is resistant to the same treatment. Differences of race, of habitat, of abundance of *Glossina*, and of virulence of the pathogenic agent undoubtedly play a part, but these factors are not the whole explanation. The drugs seem to have lost their power to sterilize rapidly the blood of carriers in certain districts, and lumbar puncture of 5-year-old cases in apparently excellent health shows that about a quarter of them exhibit meningeal changes. [It is possible that the difficulty in sterilizing the infected in the old foci of the disease may be due to the fact that prolonged treatment of the disease in these areas has resulted in the production of "arsenic fast" strains of trypanosomes which are now being propagated by *Glossina*.]

W. Y.

BERTRAND (Yves). Résultats de 601 ponctions lombaires effectuées dans une région à maladie du sommeil (Nord-Togo). [Results of 601 Lumbar Punctures in a Sleeping Sickness District.]—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 522–526.

The paper is an analysis of the results provided by 601 lumbar punctures in the Lassa canton of the Pagouda sleeping sickness sector of North Togoland.

The total population examined was 11,023 and of these 5.3 per cent. had trypanosomes in the glands or blood. Lumbar punctures were made in 601 cases : of these 364 were new patients with parasites in

the blood or glands, but not somnolent ; 26 were new cases with parasites in the blood or glands, and somnolent ; 120 were old cases 4 years under treatment and in good condition ; and 91 were suspected cases of sleeping sickness but with negative blood and glands.

The cerebrospinal fluid was examined in respect of :—(1) cytology, (2) protein content, and (3) the colloidal benzoïn reaction. The results of these examinations in each of the 4 classes of case mentioned above are given in detail, and certain deductions are drawn.

The author considers that systematic lumbar puncture practised in the bush, in conjunction with blood and gland juice examination, constitutes the only scientific method of ascertaining the nature of the virus afflicting the country. It was found that amongst new patients of healthy appearance evidence of nervous lesion existed in no less than 34 per cent. Among the old patients treated 4 years previously and in apparently excellent health 24 per cent. exhibited evidence of meningeal lesions ; as did also 14 per cent. of the suspected cases. As a general rule the positive colloidal benzoïn reaction seems to appear before the meningeal reactions ; it accompanies these reactions and is the more definite as the reactions are the more intense, and it tends to persist for some time after the reactions have disappeared. W. Y.

VAN DEN BRANDEN (F.). Contribution à l'étude de la transmission héréditaire du *Trypanosoma gambiense* chez l'homme. [The Question of Hereditary Transmission of *T. gambiense* in Man].—*Ann. Soc. Belge de Méd. Trop.* 1934. June 30. Vol. 14. No. 2. pp. 199–201.

After briefly summarizing the scanty literature relating to this subject, the author mentions an instance in which hereditary transmission did not occur although all the conditions appeared to be very favourable.

A woman from Bumba was admitted to the hospital at Leopoldville in an advanced state of pregnancy. The peripheral blood contained numerous trypanosomes and the spinal fluid showed great excess of lymphocytes and of protein. She was delivered of a normal child two days after admission. Examinations of the infant's blood made on several occasions failed to reveal the presence of trypanosomes.

W. Y.

ELLIS (M.). A Report on the Effect of Tryparsamide on Sleeping Sickness Cases.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 207–208.

The author has examined the effect of a course of tryparsamide on the peripheral infection in a large number of cases of sleeping sickness in Northern Nigeria.

The work was carried on in the Kirikasamma district of the Hadeija Emirate, Northern Nigeria ; it was undertaken in conjunction with Government mass survey and treatment. The positive cases (glands or blood) found during this survey were treated with a course of tryparsamide consisting for adults of 13 injections at 5-day intervals, the first dose being 1 gm. and the subsequent dose 2 gm. each. On the morning of the last injection all the cases under treatment were re-examined in exactly the same way as in the original survey. The results can be summarized as follows :—

Findings at the initial survey :—

Gland juice positive	717
Blood positive	112
Total	829

Findings after 12 injections (23 gm.) of tryparsamide :—

(a) Cases with glandular enlargement :—

Puncturable	239
Too small for puncture	212
Total	451

Cases with no glandular enlargement 378.

(b) Positive findings of trypanosomes :—

Gland juice	2
Blood	13
Total	15=1.81 per cent.

It is recorded that of these 15 positive cases 14 were originally diagnosed by gland juice examination and one by blood examination. After the course of treatment, 7 of these 15 cases exhibited glands large enough for puncture, whilst in 8 the glands were too small for puncture.

The conclusions are as follows :—

1. In this series of cases, 1.81 per cent. were resistant to tryparsamide.
2. In a majority of cases, tryparsamide causes a subsidence of the swelling of the posterior cervical glands.
3. The disappearance or the persistence of the glandular swelling is no criterion of cure by tryparsamide.
4. Tryparsamide is very lethal to trypanosomes in gland-juice, only two out of 717 cases still showing them after treatment."

W. Y.

BONNET (M.). Sur l'efficacité de la tryparsamide chez les trypanosomés en 2e période. [The Efficacy of Tryparsamide in the 2nd Stage of Sleeping Sickness.]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 659-663.

This note is a criticism of a recent paper by LORÉ and MARTY, who express the opinion that those cases of sleeping sickness which have been treated with tryparsamide when in the first stage of the disease are found to be resistant to this drug when they have passed into the second stage [this *Bulletin*, Vol. 31, p. 202].

Doubtless in a region where trypanosomiasis has been treated in as intensive a manner as in the Cameroons, a certain degree of resistance of the virus to the trypanocidal action of drugs will be observable after some years; but it will be an arsenic-resistance, and consequently a resistance to atoxyl and other arsenicals as well as to tryparsamide. It is, however, difficult to test the point in the second stage cases, because tryparsamide alone is active, and is used, in such patients.

Moreover, Bonnet argues that the observations published by LORÉ and MARTY do not provide proof that the cases were actually tryparsamide resistant. The two groups of cases are not comparable.

Group A consists of a residue of old cases sent to Ayos because previous treatment had failed, whereas Group B consisted of freshly discovered cases which had not previously had tryparsamide or any other form of arsenical treatment. This fact seems sufficient in Bonnet's opinion to explain the great mortality observed in the first group. Then there is nothing to prove that the patients of Group A were first stage cases when they were first discovered. Furthermore, many of the Group A patients did not receive tryparsamide for a long time after their discovery. Of the 10 cases 8 were diagnosed between 1923 and 1926, and it is known that in the Cameroons tryparsamide came into general use only in May, 1927. Before this date they were treated with atoxyl or novarsenobenzol and they had progressed into the second stage.

In short, the only thing certain about the patients of Group A is that they had been given tryparsamide before they were lumbar punctured; it is absolutely impossible to state whether they were in the 1st or 2nd stage when tryparsamide was given, and consequently it is impossible to assume an acquired resistance to tryparsamide.

Bonnet then proceeds to give illustrations from his own experience and from that of others, which, in his opinion, prove that it is not a resistance to tryparsamide, acquired as the result of using this drug in the first stage, which explains the therapeutic failures obtained in certain cases. He re-examined the protocols of 156 sleeping sickness patients who died at Ayos in 1932. Of these 94 were old cases corresponding to Group A of LORÉ and MARTY and 62 were second stage patients who had never previously been treated (Group B). The fact that 40 per cent. of these fatal cases belonged to Group B showed that the therapeutic failure was not due to tryparsamide resistance.

Bonnet does not entirely agree with LORÉ and MARTY when they write that tryparsamide should never be used in first stage cases, as some of these, which cannot be successfully treated by atoxyl or orsanine, yield to tryparsamide; nevertheless in the majority of cases tryparsamide should be reserved for the nervous period. W. Y.

- i. MILLOUS (M.) & MAURY (M.). Sur le traitement de la trypanosomiase au Cameroun par la tryparsamide. [*The Treatment of Trypanosomiasis in Cameroons by Tryparsamide.*]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. p. 665.
- ii. MARTY (M.). Sur le traitement par la tryparsamide des trypanosomés en 2e période. [*The Treatment of Second Stage Trypanosomiasis by Tryparsamide.*]—*Ibid.* pp. 663-664.

i. In commenting on the paper of LORÉ and MARTY [this *Bulletin*, Vol. 31, p. 202], Millous and Maury state that arsenic resistance appears to be a general phenomenon due to a too cautious use of insufficient doses of trivalent or pentavalent arsenicals owing to the fear of producing ocular accidents. They quote the reviewer as stating that "salvarsan-resistance or atoxyl-resistance implies tryparsamide resistance," but apart from this they consider the statements of LORÉ and MARTY are open to other objections. There seems no evidence that Group A cases were in the first stage at the first time of treatment with tryparsamide. In reality they were a collection of patients who were given tryparsamide before they were punctured, which is, of course, quite a different thing.

ii. Marty replies to the above criticisms. He does not admit that he and LORÉ were in error when they classified their Group A patients

as being first stage cases. The original treatment they were given—1 dose of atoxyl and 12 doses of tryparsamide—was at that time the standard treatment for sterilizing the infection and not for nervous cases. The clinical records contain nothing suggesting that the patients had passed into the second stage of the disease. He adheres to the conclusion of LORÉ and himself that it was the administration of tryparsamide before the appearance of meningeal lesions which was responsible for the special resistance exhibited later. W. Y.

LIEURADE (L.). L'urotropine intraveineuse associée aux arsenicaux dans le traitement de quelques cas de trypanosomiase en 2e et 3e périodes. [**Urotropine Intravenously associated with Arsenicals in the Treatment of 2nd and 3rd Stage Sleeping Sickness.**—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 438-443.

Details are given concerning 12 advanced cases of sleeping sickness treated by urotropine and tryparsamide.

The urotropine was given intravenously in doses of 2 to 3 cgm. per kilo. at weekly intervals about 3 hours before the arsenical. Albuminuria and an increase of protein in the cerebrospinal fluid was almost always observed on the following days, but, as a rule, disappeared before the next dose was due. The results obtained were satisfactory in 6 cases, but unsatisfactory in the remainder. The author remarks [and with justice] that it might be argued that the good results were due to the tryparsamide alone: he, however, is of opinion that the association of urotropine with tryparsamide had accelerated and accentuated the beneficial results. W. Y.

RAINGEARD. Traitement par l'hyposulfite de soude des troubles oculaires dus aux trypanocides. [**Sodium Hyposulphite in the Treatment of Ocular Troubles due to Trypanocides.**—*Rev. Méd. et Hyg. Trop.* 1934. May-June. Vol. 26. No. 3. pp. 143-153.

An interesting, and possibly important, paper in which the author records the beneficial results he has obtained by the use of sodium hyposulphite in cases of trypanosomiasis treated with atoxyl or tryparsamide, who developed ocular troubles.

Details of the treatment of 26 such cases are given and the results are summarized in the table here reproduced.

It thus appears that in this series of 26 cases there were no less than 77 per cent. of successes, and in the 12 blind cases treatment was successful in no less than 9 cases. The successful results were not limited to recent cases, but were obtained also among those who had been blind or semiblind since 1928 to 1930.

Discussing the best dosage, the author points out that his results were most favourable in the group of cases which were given 15 injections on alternate days, each of 10 cc. of a 20 per cent. solution intravenously. It is emphasized that all these cases, with a single exception, were given tryparsamide treatment only after the course of hyposulphite, and consequently there is no doubt that it was the latter drug which caused the ocular improvement. The author points out that he did not examine the eyes with the ophthalmoscope as his work was carried out in the bush, but he emphasizes the essential fact that these people who had not been able to see for periods varying for from 2 to

Series.	Name	Age	First appearance of accidents		Treatment used		Sight very poor.	Almost Blind.	Blind.	Improvement.	Great improvement.	Recovery.	Success.	Failure.
			Old cases	New 1933	Ato- xyl	Tryp								
I	Elindi ...	55		+		+			+		+		+	
	Noumbi ...	38	+32		+			+			+		+	
	Liniebe ...	33	+30		+		+				+		+	
	Totole ...	35	+30		+			+		+			+	
II	Mangoumbo ...	26	+20		+				+					+
	Matende ...	33	+31			+			+				+	
	Kanga ...	34	+29		+		+			+			+	
	Mipoudi ...	38	+29		+			+				+	+	
	Doumba ...	32	+31		+			+				+	+	
	Badondo ...	40	+28		+			+					+	+
	Mwele ...	35	+28		+			+	+				+	
	Bombo... ..	30	+28		+			+					+	+
	Boudzanga ...	36	+32		+				+	+			+	
III	Awe ...	35	+32			+		+				+	+	
	Dimeka ...	34	+31			+		+				+	+	
	Lele ...	35	+32			+			+			+	+	
	Manzamba ...	38		+		+	+					+	+	
	Alama ...	28	+31			+		+	+			+	+	
	Bangwa ...	32		+	+			+						+
	N'Danga ...	36		+	+				+					+
IV	Souangala ...	32		+	+		+		+			+	+	
	Mangoumba ...	35		+	+							+	+	
	Daminene ...	58		+	+		+				+		+	
	N'Koho ...	25		+	+		+						+	
	Nanha ...	32		+		+	+					+	+	
	Maniebe ...	32		+		+	+					+	+	
	26		16	10	17	9	8	6	12	5	4	11	20	6
Percentage of cured			76.84 per cent.					
" uncured			23.07	"				

even 5 years recovered within a few weeks a degree of vision which enabled them to get about and attend to their needs. [As the author himself freely admits, this work should be repeated on a sufficiently large scale.] W. Y.

LASSABLIÈRE (P.) & PEYCELON (A.). Action de l'iodo-bismuthate de quinine sur le *Trypanosoma gambiense*. [Action of Quinine Iodo-Bismuthate on *T. gambiense*.]—*Rev. Méd. et Hyg. Trop.* 1934. May-June. Vol. 26. No. 3. pp. 129-137.

A considerable number of guineapigs infected with a strain of *T. gambiense* were treated with quinine iodo-bismuthate.

A soluble and an insoluble form of the compound were used; the former was injected intramuscularly and also subcutaneously, the latter only subcutaneously. The results which are given in detail are poor, a prolongation of life being the utmost obtained. The earlier the animals were treated after infection the better the results; and the author believes that it is best to give numerous small doses at short intervals rather than fewer large doses at longer intervals.

The author concludes with the statement that the substance must be regarded as a valuable adjuvant in the treatment of trypanosomiasis, although its therapeutic action is not comparable to that of the arsenicals. [From the data presented this conclusion appears to the reviewer distinctly optimistic.] W. Y.

KEEVILL (A. J.). **Subsequent Histories of Six Cases of *Trypanosoma rhodesiense* Infection treated with "Bayer 205" or "Fournneau 309."**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. pp. 101-102.

This paper gives the subsequent histories of six cases of sleeping sickness treated only with "Bayer 205" and reported upon by the author in 1928 [this *Bulletin*, Vol. 25, p. 795].

In the first report it is pointed out that six patients with trypanosomes in the spinal fluid had, as the result of treatment with "Bayer 205" or "Fournneau 309" only, all remained in normal health for at least two years. The patients have been followed up carefully and their histories are shown in a Table; no further treatment had been given to any. It is seen that three of the patients (Cases 80, 85 and 86) have remained in normal health more than 8 years since infection. Of the three who died one (Case 91) survived two years and three months, one (Case 97) 5 years, and one (Case 72) 8 years after infection. The causes of death are not known, although the history suggests that Case 91 died of pneumonia. The long survival periods—5 and 8 years—make it highly improbable that the cause of death of either of the others was sleeping sickness. The longest survival period encountered by the author was in the case of a patient who had continuous treatment for 4 years and 8 months, and who undoubtedly died of sleeping sickness.

Three similar cases occurred among Keevill's 1926 patients with known survival periods of 4, 6, and 8 years, and with in each case a return to normal of the spinal fluid.

Keevill emphasizes the fact that these cases are recorded as a matter of interest only, and that it is now widely recognized by all with experience that in cases in which trypanosomes are found in the spinal fluid reliance on "Bayer 205" alone is quite unjustified, and that all such should be treated subsequently with tryparsamide.

W. Y.

SICÉ (A.) & MERCIER (H.). Contribution à la posologie du moranyl dans le traitement de la trypanosomiasse humaine à *Tr. gambiense*. [The Dosage of Moranyl in the Treatment of Gambiense Sleeping Sickness.]—*Marseille-Méd.* 1934. Feb. 25. Vol. 71. No. 6. pp. 301-308.

This article is concerned with the question of how moranyl can be most usefully employed in human trypanosomiasis due to *T. gambiense*.

The authors state that certain investigators, especially the English, give the drug intravenously to the exclusion of all other remedies; each injection consists of 1 gm. and the dose is repeated 10 times at weekly intervals. Other workers, particularly the Germans, prefer to give 3 or 4 large doses at 2-day intervals.

The authors' experience was obtained at the Pasteur Institute of Brazzaville, where two different lines of treatment were followed. The first group of patients, who had not before received any treatment, were given moranyl alone; in the second group of patients the drug was used to control certain blood relapses, which occurred in patients undergoing long courses of treatment with orsanine or tryparsamide.

The results obtained with the first group of patients showed that moranyl given orally or intravenously in 8 weekly doses of 1 gm. had a sterilizing effect equal to that of orsanine; but it had the great disadvantage of producing an albuminuria which was sometimes serious.

VAUCEL has used moranyl in cases of sleeping sickness in the meningeal stage, and also for blood relapses in cases treated with arsenicals [this *Bulletin*, Vol. 28, p. 905]. Some meningeal cases improve greatly under arsenical treatment, but suffer from blood relapses, and VAUCEL found that moranyl is useful in certain of these cases; but in those cases which show evidence of persistence of the meningeal symptoms moranyl was useless.

The authors record in detail two cases of nervous trypanosomiasis in which moranyl was combined with tryparsamide. The moranyl was given orally, on an empty stomach on waking in the morning, in a dose of 0.5 gm. An intravenous injection of 1.0 gm. of tryparsamide was given later in the morning. This treatment was given on 7 occasions at 3-day intervals. The results were favourable so far as the observations extend and only slight and transient albuminuria was occasionally seen.

W. Y.

VON JANCsó (N.) & VON JANCsó (H.). Mikrobiologische Grundlagen der chemotherapeutischen Wirkung. I. Mitteilung: Wirkungsmechanismus des Germanins (Bayer 205) bei Trypanosomen. [**Mode of Action of Germanin in Trypanosomiasis.**—*Zent. f. Bakt.* I. Abt. Orig. 1934. Sept. 3. Vol. 132. No. 5/6. pp. 257-292. With 12 figs. [52 refs.]

This long and interesting paper is concerned with the mechanism of the therapeutic action of "Bayer 205" in trypanosomiasis.

The authors point out that previous attempts to demonstrate *in vitro* a trypanocidal activity of "Bayer 205" at all comparable with its amazing activity *in vivo* have failed, probably, as the reviewer has pointed out, because a technique has yet to be developed whereby the pathogenic trypanosomes could be maintained *in vitro* in a state of unlowered vitality for a sufficiently long period for the action of "Bayer 205" to become manifest. After referring to the previous attempts to develop a satisfactory technique for keeping trypanosomes alive *in vitro*, von Jancsó describes his own, which is essentially a modification of that described by the reviewer and his colleagues [this *Bulletin*, Vol. 27, p. 237].

As a rule sheep serum was used; the blood was defibrinated and then centrifuged. The serum, after being kept for a day in the ice-chest and diluted with an equal volume of Ringer solution, was filtered through a Seitz-E.K. filter. The filtration was not merely for the purpose of sterilizing the serum, but because it was found that it actually improved the serum as a nutrient medium. The filtrate was then deactivated at 60°C. for 40 minutes. Flasks made of Vitrex-glass were used in the processes, and were closed with first quality cotton wool; they were sterilized at 130°C. for several hours.

A sterile solution of 0.02 per cent. solution of glucose in physiological saline was next prepared, and 10 cc. of the serum-glucose Ringer solution was added to each 100 cc. of the glucose solution so as to form the nutrient medium, which consequently contained 5 cc. of serum per 110 cc. The medium was then divided among small flasks so that each contained 50 cc. and the flasks were closed with cotton wool plugs.

The trypanosomes were obtained from the heart blood of rats, mice or guineapigs with moderately heavy infections and coagulation was prevented by heparin (Schering-Kahlbaum) 1 per cent. solution. The authors attach importance to this. After thorough mixing of the blood and heparin sufficient drops were added to the 50 cc. of medium to give a concentration of trypanosomes of between 200 and 1,000 per cmm. The flasks were then incubated at 37°C.-38°C. For the enumeration of the trypanosomes the Bürke counting apparatus was employed as the Thoma-Zeiss was found to be too small.

The authors state that with this technique multiplication of the trypanosomes could be observed for at least 6-10 hours and sometimes for much longer according to the strain used, and that the parasites remained alive in good condition for from 50 to 70 hours.

With the aid of this technique the authors were able to demonstrate *in vitro* a trypanocidal activity of germanin when its concentration was only 1 in 80,000, and that a concentration of 1 in 60,000 sufficed to destroy all the parasites. The trypanocidal effect was, however, manifest only after a prolonged latent period amounting to as much as 24 hours. During this latent period the trypanosomes showed no signs of any toxic effect, and multiplied just as rapidly as the controls. Even in high concentrations germanin exhibits no immediate toxic action on trypanosomes.

In this respect the action of germanin is strikingly different from that of such drugs as the arsenoxides which have an immediate effect. Apparently germanin acts, not by directly destroying vital functions, but by the production of athrepsis through interference with the nutrition of the trypanosomes.

The authors next turned their attention to the mechanism of the curative action of germanin *in vivo*. By means of splenectomy, and blocking the reticulo-endothelial system with electrocolloidal copper, they threw out of action the natural trypanocidal protective mechanism of the host, thus enabling the direct action of the drug to be studied in the living animal. It was found that the curative action depended upon the direct trypanocidal action of the chemically unchanged germanin molecule, but that the therapeutic process was rather more complicated than a simple internal disinfection.

Germanin possesses the important and peculiar property of rendering the slightly poisoned trypanosomes fit for phagocytosis by the reticulo-endothelial cells, *i.e.*, it exercises an opsonic effect. The disappearance of the parasites from the blood stream during the cure is due to a removal of the slightly damaged trypanosomes by the phagocytes in the blood sinuses of the liver, spleen and bone-marrow. This opsonic action thus greatly enhances the effect of the drug in the living animal and explains its greater action *in vivo* than *in vitro*. Nevertheless the drug can produce a cure without the aid of its opsonic power, because it is also curative in splenectomized and blocked animals. In such animals its activity is, however, distinctly less than in normal animals; and in some cases the chemotherapeutic index in normal animals was found to be 1:270, whilst in blocked animals it was only 1:135. Another observation in harmony with the above is the

time required to produce sterilization of the blood in the normal and in the blocked animal. In the former this is about 15 to 24 hours, but in the blocked animal in which the reticulo-endothelial system is put out of action and consequently the opsonic effect of the drug is not seen, the time required for sterilization of the blood is increased to 25-44 hours, which is approximately the same as that required for the destruction of the parasites *in vitro* by germanin.

In the blocked animals the same degenerative changes can be seen in the trypanosomes as in the *in vitro* observations. Characteristic among these is inhibition of division; giant forms with many nuclei, blepharoplasts and flagella appear. Sometimes as many as 60 per cent. of the parasites may be found to be in a state of division. In striking contrast the normal animal shows when treated with germanin but few abnormal forms, because as soon as the parasite commences to be damaged by the drug it is removed from the circulation by the phagocytes.

A somewhat similar opsonic effect is seen in the treatment of recurrent fever infections with solganal A & B. W. Y.

SINGER (Ernst), KOTRBA (Jan) & FISCHL (Viktor). Zur Frage der Kombinationstherapie. [**On the Question of Combined Therapy.**] —*Ztschr. f. Hyg. u. Infektionskr.* 1934. Aug. 16. Vol. 116. No. 3. pp. 241-247. [14 refs.]

This short and rather technical paper deals briefly with the general question of combined therapy and in particular with the question whether anything is to be gained by combining salvarsan with various heavy metals.

Ever since 1905 much attention has been devoted to the possibility of increasing the specific activity of drugs by combination. This may take one of several forms: instead of using a single drug several belonging to different chemical groups can be administered; or compounds can be synthesized which contain two active groups instead of one; or an active non-metallic compound can be combined with an active metallic salt.

With the object of throwing some light on the mechanism of action of combined therapy, the authors have considered the combination of salvarsan with inactive metallic salts, *e.g.*, coppersalvarsan and silver-salvarsan; and as representative of the combination consisting of two active compounds, they employed the complex compound formed from solusalvarsan and solganal. When solutions of these are mixed together the mixture exhibits a deep red colour in contrast to the orange yellow colour of the original solutions. The therapeutic activity of each of these compounds and of the mixture was then tested on mice infected with "*Recurrens*" and nagana respectively. It was found that the mixture exerted a definitely more powerful effect than either of the components given separately.

The authors refer to the fact that in their earlier work they had devised a colorimetric method whereby they could readily estimate quantitatively arsenic and other metals at the same time; for this purpose they used a spectrographic method. The metallic contents of copper-salvarsan, silversalvarsan and solusalvarsan-solganal are shown in the following table:—

Preparation.	Arsenic	Metal	Arsenic : Metal.
	%	%	
Coppersalvarsan	25.5	13.5 Cu	1 : 0.5
Silversalvarsan	19.5	12.5 Ag	1 : 0.6
Solusalvarsan-Solganal ...	10.0	18.3 Au	1 : 1.8

The results obtained with infected mice are shown in the next table. In each case half the tolerated dose was given intramuscularly, and the investigations were continued so long as fairly numerous parasites (10 per field) could be seen in the blood.

Mouse's blood after	Blood corpuscles in ccm.	Arsenic and metal in γ .					
		Plasma.		Blood corpuscles.		Parasites.	
		Arsenic.	Metal.	Arsenic.	Metal.	Arsenic.	Metal.
Recurrans : 1/2,000 gm.							
30 mins.	1.35	0	0	0	0	0	0
1 hour	1.3	0	0	0	0	0.5	0
Nagana : 1/2,000 gm.							
30 mins.	0.5	0	0	0	0	1.0	0
Recurrans : 1/1,200 gm.							
30 mins	0.7	3	3	0	1.2	0	0
1 hour	0.8	4	0	0	0	0.5	0
3 hours	0.5	3	0	0	0	0	0
5 "	0.9	4	0	0	0	0	0
Nagana : 1/1,200 gm.							
30 mins	0.3	20	60	3.5	2.8	0.6	0
1 hour	0.4	20	80	6.0	12.0	0.6	0.6
Recurrans : 1/1,200 gm.							
30 mins	1.2	21	62	5.0	4.0	0.6	0.2
1 hour	1.1	19	57	5.0	10.0	0.6	0.6

These experiments show that the various salvarsan compounds exhibit a great difference in regard to their distribution in the organism. Comparison of the above tables shows that neither in the body of the host nor in the parasite is the combination taken up as such, but that immediately after injection they are split up into their component parts, the destiny of which in the organism is different. It seems therefore clear that in the case of coppersalvarsan and silversalvarsan, the combined copper and silver is split off from the salvarsan immediately after injection, and consequently has no action on the parasite. This observation demonstrates the fallacy of the various hypotheses elaborated to explain the action of such substances, *e.g.*, the view that the antisyphilitic action of silver is enhanced in silversalvarsan because this compound, in virtue of the specific affinity of salvarsan for the spirochaetes, anchors, as it were, the silver to the parasites. The authors write that as a matter of fact, after an injection of silver salvarsan, the silver goes its own way in the organism and whether it has a special affinity for chancre tissue is a question for investigation, but it is rather improbable. Silversalvarsan can act as a combination drug, but only if the silver component exerts an influence on the

syphilitic infection and this has yet to be proved; copper-salvarsan cannot play a part in combined therapy because copper has no spirochaeticidal action.

The authors conclude by expressing the opinion that it seems as if combined therapy will be found to have far less significance in chemotherapy than in pharmacology.

The following summary is given:—

1. Copper-salvarsan and silver-salvarsan are split into their component parts after injection into the animal body; of the two components only the benzol derivative exerts a specific action on the parasite.

2. In contrast, a complex combination of solus-salvarsan and solganal is described, which is also split in the body of the host into its component parts, but in this case both are taken up by the parasites. The poorer therapeutic effect of the complex combination observed is probably to be regarded as an interference phenomenon.

3. Spectrographic analysis established that these are different kinds of combination therapy. W. Y.

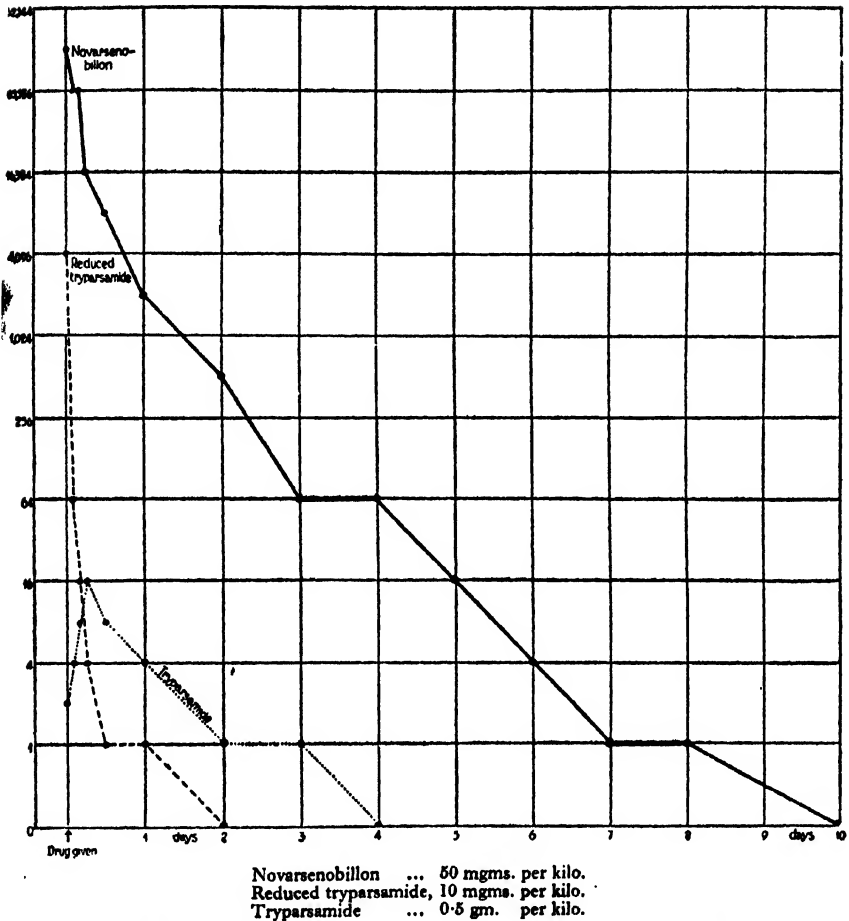
MURGATROYD (Frederick), RUSSELL (Helen) & YORKE (Warrington). **Studies in Chemotherapy. XI.—The Trypanocidal Titre of the Serum of Rabbits after the Intravenous Injection of Various Compounds of Arsenic.**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 227–242. With 4 graphs.

Many workers have studied the problem of the length of time a drug remains in the blood after intravenous injection, but as far as the arsenicals are concerned, with not much success. The work has consisted in the quantitative estimation of arsenic in the blood, organs and excreta at stated intervals, but this method does not tell us whether the arsenic is in the blood in the form in which it was injected, or is broken down in the body, *e.g.*, whether salvarsan and tryparsamide circulate in the blood as such or are changed before they exert their specific effects, nor in what form they are eliminated.

In continuation of their previous researches the authors' object was to ascertain the trypanocidal power of the serum of rabbits after the intravenous injection of novarsenobillon, reduced tryparsamide thioglycollate and tryparsamide—typical examples of arsenobenzol compounds, aromatic trivalent and aromatic pentavalent arsenical compounds. The method essentially was the determination of the trypanocidal titre of the rabbits' serum by incubation at 37°C. of trypanosomes in nutrient medium containing various concentrations of the serum. For details of the technique the paper must be read. The results are described in the authors' summary.

"1. Attention is drawn to the fact that there is practically no information regarding the length of time an arsenical compound remains in the blood after intravenous injection. Such information as we do possess depends upon chemical estimations of arsenic and, for reasons which are discussed, is quite inadequate for the solution of many important questions.

"2. With the object of throwing further light on the subject a technique was devised which has enabled us to follow the variations in the trypanocidal titre of the serum after intravenous injection of rabbits with different doses of each of the three types of aromatic



Graph comparing the trypanocidal titre of the serum of rabbits after moderate doses of novarsenobillon, reduced tryparsamide, and tryparsamide respectively.

[Reproduced from the *Annals of Tropical Medicine and Parasitology*.]

arsenical compounds, viz., arsenobenzol, trivalent arsenical and pentavalent arsenical compounds.

" 3. The effect of injection of the arsenobenzol and trivalent arsenical compounds is to confer immediately upon the serum an enormously high trypanocidal titre. This titre, which is proportional to the dose given, immediately falls—quickly at first and more slowly later—until it ultimately returns to zero. The only difference observed in the effect of the two compounds is that the fall in titre in the case of the trivalent compound is much more rapid than in that of the arsenobenzol compound.

" 4. The immediate effect of injection of the pentavalent compound is to confer but a slight trypanocidal titre upon the serum. Instead of falling, however, as happens with the other two drugs, the titre steadily rises and does not attain to its maximum until approximately 6 hours

after the injection. The titre reached is, moreover, in no way comparable with the enormous titres obtained with the arsenobenzol and trivalent compounds.

"5. Analysis of the observations made in this work suggest that the arsenobenzol and trivalent arsenical compounds owe their therapeutic activity entirely to the fact that these highly trypanocidal substances circulate unchanged in the blood stream; and that tryparsamide owes its therapeutic activity to the fact that it is gradually reduced in the blood, and possibly also in the tissues, into its corresponding trivalent compound."

Elsewhere they write :—

"We have already drawn attention to the remarkable speed with which the trivalent compounds escape from the blood; and, consequently, we can explain the fact that the trypanocidal titre following an injection of tryparsamide never rises beyond very modest limits (maximum observed about 128) on the ground that as fast as the tryparsamide is reduced to its trivalent form it is eliminated from the blood stream. Whether the reducing process occurs elsewhere than in the blood stream, *e.g.*, in the reticulo-endothelial cells, we do not know. Neither do we know whether the tryparsamide, which is taken up by the body cells immediately after injection of the drug, is after an interval returned to the blood stream as such, or whether it is retained in these cells until it is ultimately broken down into some simple and possibly inactive form."

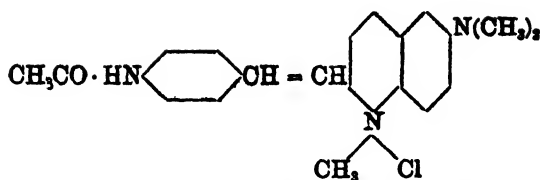
A. G. B.

BROWNING (C. H.) & GULBRANSEN (R.). **Prophylaxis of Experimental Trypanosome Infections by Chemotherapeutic Agents.**—*Jl. Path. & Bact.* 1934. July. Vol. 39. No. 1. pp. 75-82.

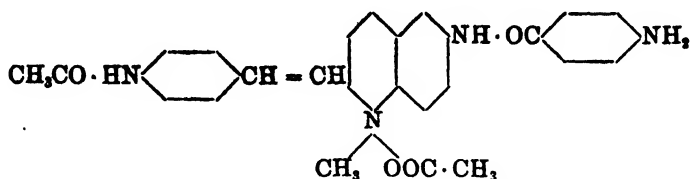
This paper is concerned with the mode of action of drugs which are known to exert a prophylactic action against trypanosomal infections.

The authors point out that the trypanocidal drugs which exhibit pronounced prophylactic action are "Bayer 205" and certain benzoyl-amino quinoline styryl compounds (Nos. 245, 430 and 437 of Browning, Cohen *et al*, 1933). It is considered that prophylactic action may be due to several properties of a drug.—(1) Its excretion or destruction may occur so slowly that it circulates for a long time in the body; (2) it may form a relatively insoluble local deposit in the tissues from which small amounts continually pass into the body fluids to act upon the parasites; or (3) although rapidly excreted or destroyed the drug may act as a stimulus leading to a persistent elevation of the defensive powers of the tissue. There is, however, no evidence in support of the last mode of action.

With the styryl quinoline compounds, striking prophylactic action is associated with the presence of p-amino benzoyl (or p-dimethyl-amino benzoyl or p-acetyl-amino benzoyl) substituted in the 6-NH₂ group of the quinoline nucleus [*vide* styryl-245], and such compounds are slowly absorbed. On the other hand the analogous trypanocidal substances in which the 6-position is occupied by —N(CH₃)₂ [styryl-90] or —NH·OCH₂C (styryl-8) are rapidly absorbed and excreted after subcutaneous injection and exert only a brief prophylactic action.



2(p-acetyl-amino styryl)-6 dimethyl-amino quinoline methochloride (styryl-90)—
prophylactic action brief.



2(p-acetyl-amino styryl)-6(p-amino benzoyl-amino) quinoline methoacetate
(styryl-245)—prophylactic action prolonged.

In their experimental work the authors used three strains of *T. brucei* obtained from MESNIL and one strain from WORMALL in Uganda. In two tables the prophylactic action for mice of Bayer and of styryl-245, respectively, are shown. With "Bayer 205" it was found that 1 cc. of a 1 in 200 solution protection lasted less than 3 months and after a dose of 1 in 1,000 solution about 2 months. Experiments with styryl-245 showed that 1 cc. of a 1 in 200 or 1 in 250 solution confers on mice longer protection than any other known substance. In some cases complete protection for almost a year was observed.

The authors state that styryl-245 owes its protective power to the fact that when a watery solution is injected subcutaneously a local deposit forms, which is accompanied by considerable reaction of the connective tissue elements; the dye is fixed intracellularly to a great extent and still persists at the site after a year or longer. The amount in circulation at any time is very minute, but nevertheless sufficient is absorbed to prevent infection on subsequent inoculation with trypanosomes, or, when the drug is injected after inoculation, to cure the established infection.

W. Y.

CHRISTISON (May H.). Ueber chemotherapeutische Versuche bei der Rattentrypanose (*Trypanosoma lewisi*). [**Chemotherapeutic Experiments on *T. lewisi* Infected Rats.**—*Zent. f. Bakt.* I. Abt. Orig. 1934. Aug. 7. Vol. 132. No. 3/4. pp. 228-237. [34 refs.]

The paper contains a summary of the therapeutic results obtained with 21 pyridin compounds of arsenic and with certain other substances, including two arsenostibio-compounds, on infections due to *T. brucei*, *Spirochaeta crociduræ*, *Bac. rhusiopathiæ* and *T. lewisi*, respectively.

Of the arsenopyridin compounds only one, viz.: Br 23, i.e., 2-pyridon-3-amido-5 arsinic acid exercised a weak action on *T. lewisi* infections. The arsenostibio-compound Sdt 386 B, which is so active in Bartonella infections, likewise exerted only a slight action on *T. lewisi*.

W. Y.

BROWNING (C. H.), CAPPELL (D. F.) & GULBRANSEN (R.). **Experimental Infection with *Trypanosoma congolense* in Mice: the Effect of Splenectomy.**—*Jl. Path. & Bact.* 1934. July. Vol. 39. No. 1. pp. 65-74. [19 refs.]

As a preliminary to studying the chemotherapy of *T. congolense* infections the authors have passed a strain of the parasite repeatedly through mice with a view to accommodating it so far as possible to this host, and they have also examined the effect of splenectomy and blockade.

Extended observations over several hundred passages in mice showed that the parasites were incapable of developing the high virulence for that species which is characteristic of *T. brucei*. Many of the mice of the first 50 passages failed to become infected. From the 83rd passage onward infection always occurred, but in only about a fourth of the animals was there a progressive increase of the parasites and the infection took an acute course; in the remainder the infection took a relapsing, or, less frequently, a chronic course. The incubation period was but slightly shorter in the later passages than in the earlier ones.

The animals which resisted the first large inoculations were shown to be abnormally resistant as tested by their behaviour on reinoculation, but after repeated re-inoculations they finally became infected. Spontaneous cure was very rarely seen.

Neither splenectomy nor combined splenectomy and blockade with iron sugar produced any definite alteration in the course or severity of the infection of *T. congolense* in mice. W. Y.

CORSON (J. F.). **The Infectivity of *Trypanosoma rhodesiense* in Relapses after Treatment with "Bayer 205."**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 225-226.

The experiment described in this paper was undertaken with the object of throwing light on the question whether in sleeping sickness the blood during relapses after "Bayer 205" can infect tsetse flies.

In order to eliminate doubt about relapse or re-infection in the case of natives, it would be necessary to detain them in a fly-free place until a blood relapse occurred. Owing to the temporary absence of facilities for doing this, the author thought it worth while to make an experiment with laboratory animals.

A rat was bitten by a tsetse fly infected with *T. rhodesiense* on February 18th, and trypanosomes appeared in its blood on the 5th day onwards. On 5th March the blood was inoculated into 3 rats, all of which became infected. Fourteen days later, when trypanosomes were numerous in the blood, each of these 3 rats was given a subcutaneous injection of 0.02 gm. of "Bayer 205" per kilo. of body weight. The trypanosomes disappeared from the peripheral blood in each case from March 21st to 24th, reappearing on March 25th for a few days and again disappearing for various periods. On March 28th other rats were sub-inoculated from these 3 animals and all became infected. Laboratory-bred *G. morsitans* and *G. palpalis* were fed on the first 3 rats on March 27th, 28th and 29th, and afterwards on a clean rabbit. On April 17th the flies were transferred to a clean guinea pig which became infected.

These experiments show that *T. rhodesiense* in rats, during a relapse after treatment with "Bayer 205," was transmissible both by direct inoculation and by cyclically infected tsetse flies. W. Y.

DUKE (H. Lyndhurst). **On the Transmissibility by *Glossina* of *Trypanosoma brucei*, *T. rhodesiense* and *T. gambiense*, with Special Reference to Old Laboratory Strains.**—*Parasitology*. 1934. June. Vol. 26. No. 2. pp. 153–162. [14 refs.]

This paper records the result of an investigation of the transmissibility of certain strains of trypanosomes of the polymorphic group; it deals particularly with strains which have been maintained for a long period in the laboratory away from any contact with tsetse.

In his historical introduction Duke points out that BOUER and ROUBAUD (1910) found that they could not transmit by *Glossina* strains of *T. brucei*, *T. evansi*, and *T. gambiense*, which had been obtained from the Pasteur Institute in Paris. KLEINE and FISCHER (1913) in East Africa were unable to transmit certain strains of *T. gambiense* by *Glossina*. REICHENOW (1921) reported that certain strains of *T. gambiense* in man himself were not transmissible, and during recent years much work has been done on this subject by Duke himself.

The strains examined in the present work were as follows:—

- No. 1. *T. gambiense*, strain V. First isolated from man early in 1926 and found to possess an unusual degree of transmissibility by *G. palpalis*.
 No. 2. *T. gambiense*, strain "Adero." Isolated from a native of the Uganda Protectorate in January, 1933.
 Nos. 3 and 4. *T. rhodesiense*, "Liverpool" strain. This was sent to Duke by the Reviewer. It was isolated from man in 1923, and the arsenic-fast variant, No. 4, was prepared in Liverpool.
 No. 5. *T. brucei*, strain "Hamburg alt." This is the strain used by Schilling and Schreck (1930) in their work on the stability of acquired characters in trypanosomes, experiments performed in 1912–14 and published in 1930. The remarkable feature of Schilling's work with this strain appears to be the ease with which it was passed through tsetse. The Reviewer has already commented on this curious fact [this *Bulletin*, Vol. 28, pp. 894–5].
 No. 6. *T. gambiense*, strain "Braun." Isolated at Hamburg in February, 1920, from a patient from Fernando Po.
 No. 7. *T. gambiense*, strain "McA." Supplied by Professor Thomson and isolated from a European in November, 1921.
 No. 8. *T. brucei*, strain "Hornby mild." Isolated in October, 1930, from an ox by Mr. Hornby at Mpwapwa.
 No. 9. *T. brucei*, strain "Hornby virulent." Isolated from a heifer in April, 1927.
 No. 10. *T. gambiense*, strain "Br." Supplied by Professor Thomson and isolated from a European in June, 1930.

Duke summarizes the result of his work as follows:—

"1. The following strains produced no infection in any of the laboratory-bred *Glossina* used in their examination; the total number of flies dissected is given for each strain:—

<i>T. gambiense</i> , strain V, Uganda, isolated in 1926	...	548
<i>T. gambiense</i> , strain Adero, Uganda, isolated in Jan., 1933	...	1,642
<i>T. rhodesiense</i> , Liverpool, isolated in Jan., 1933	...	750
<i>T. rhodesiense</i> , Liverpool, arsenic-fast variant	...	1,166
<i>T. brucei</i> , "Hamburg alt" from Berlin; isolated over 30 years ago	...	2,452

"Some of the flies used in testing each of these strains were kept at 95–97°F. during their infecting feeds.

" 2. *T. gambiense*, strain 'Braun,' isolated in February, 1920, gave two 'gut only' infections in 1,137 flies. *T. gambiense*, strain 'McA,' isolated in 1921, produced one very light infection, of the intestinal tract only, in 1,410 flies employed. This infected fly died on the 27th day after its infecting feed.

" *T. brucei*, strain 'Hornby mild,' isolated at the end of 1930, gave three infections of the intestinal tract only in 1,443 flies used. Some of the flies employed on these three strains were kept during their infecting feeds at 95-97°F., but the infected flies came from boxes kept at room temperature throughout.

" It will be seen that all the strains hitherto summarized are, as far as these tests are concerned, non-transmissible by *Glossina*, and the majority are no longer capable of infecting even the intestine of the fly.

" 3. *T. brucei*, strain 'Hornby virulent,' isolated in April, 1927, from a heifer, and found by Corson in 1931 to be readily transmissible by *G. morsitans* or *G. pallidipes* (or both), 4½ years after its first isolation (Corson, 1932). A month or so later this strain was found at Entebbe to be still feebly transmissible by *G. palpalis* and somewhat more readily by *G. morsitans*, although much less so than in Corson's experiments.

" 4. Strain 'Br,' considered by Prof. J. G. Thomson to be a *T. gambiense* showing some resemblances to *T. rhodesiense*, when examined at Entebbe some three years after its isolation from a European in West Africa, proved to be still infective to both *G. palpalis* and *G. morsitans* though only very feebly transmissible. 4,272 laboratory-bred flies were used in the examination of this strain: 74 of these developed infection of the intestine, and only one a gland infection—a *G. palpalis* dying on the 40th day after its infecting feed. Flagellates were numerous in the glands of this fly.

" 5. The behaviour of the 'Hornby virulent' strain of *T. brucei* and of strain 'Br.' suggests that completion of the cycle in the fly may be delayed beyond the 25-30 days usually sufficient for East African strains, and it is possible that this delay may be a feature characteristic of strains whose transmissibility by tsetse is undergoing reduction. On the other hand, the solitary infective fly obtained with strain 'Br.' had a heavy gland infection which had in all probability been present at least for several days before the death of this insect.

" 6. A strain freshly isolated from a native who was infected on or near the northern shores of Lake Victoria failed to infect any of 1,642 *G. palpalis* used in its examination, although a number of these flies were kept at 95-97°F. during their infecting feeds.

" 7. The results of the investigations described in this paper lend some support to the opinion already formed as the result of numerous experiments with the polymorphic group of trypanosomes, namely that *T. brucei* (and, as far as can be seen, *T. rhodesiense*) is less prone than *T. gambiense* to lose touch with *Glossina*.

" It may be that the stability of this character in *T. brucei* is an expression of a more perfect adjustment to environment than is possessed by *T. gambiense*; the latter trypanosome, which is essentially dependent on man, having not yet attained biological equilibrium in this its principal mammalian host."

W. Y.

DUKE (H. L.). Studies on the Factors that may influence the Transmission of the Polymorphic Trypanosomes by Tsetse.—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. p. 244.

This note draws attention to an omission in a previous paper by the author [this *Bulletin*, Vol. 31, p. 565]. In the paper in question the description of the maintenance of Strain XXXIII opens with

the statement: "In the main series this strain underwent 10 consecutive cyclical passages." Actually the Table only shows 8 passages. In the present note the Table is completed, showing that the strain was cyclically transmitted through two more monkeys. The extra evidence confirms, in the author's opinion, the reduction in transmissibility suggested by the behaviour of the trypanosomes in the two previous monkeys and is therefore important to the thesis of this particular study.

W. Y.

DUKE (H. Lyndhurst), METTAM (R. W. M.) & WALLACE (J. M.). **Observations on the Direct Passage from Vertebrate to Vertebrate of Recently Isolated Strains of *Trypanosoma brucei* and *Trypanosoma rhodesiense*.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. pp. 77–84. [29 refs.]

This paper contains observations on the direct passage from vertebrate to vertebrate of recently isolated pathogenic trypanosomes. It is divided into three sections each dealing with a different mode of transmission.

i. *Transmission of T. brucei to healthy cats as a result of digestion of carcases of infected rats.*—BRUCE (1897) was the first to show that an animal might contract trypanosomiasis as a result of devouring blood or flesh of a nagana carcase; and this observation was soon confirmed by numerous other workers. Duke's experiments consisted in feeding two kittens with the carcases of rats, the blood of which swarmed with *T. brucei*. Both kittens became infected and parasites were first discovered in their blood in 11 and 12 days respectively.

ii. *Direct transmission by Stomoxys and Glossina.*—A brief summary is given of previous work on this subject. Duke himself found that *T. rhodesiense* was readily transferred from an infected to a healthy monkey by the process of interrupted feeding; 7 to 10 wild *Stomoxys* were used in the experiment.

iii. *The passage of T. rhodesiense through the placenta.*—Five guineapigs with *T. rhodesiense* in their peripheral blood gave birth to young which were found to be infected. The young of another guineapig born 3 days after the date of the infection of the mother (by fly bite) did not become infected, although they were suckled by the infected parent until her death. Three guineapigs infected with *T. gambiense* for 40 days before parturition produced healthy young.

Experiments designed with the object of determining whether fleas and lice can act as mechanical vectors of *T. brucei* produced negative results.

W. Y.

CORSON (J. F.). **The Cerebro-Spinal Fluid of Some Small Antelopes Infected with *Trypanosoma rhodesiense*.**—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 243–244.

In this note the author records the results of the examination of the cerebrospinal fluid of 8 adult dik-diks and one young duiker experimentally infected with *T. rhodesiense*. The cerebrospinal fluid was obtained by suboccipital puncture either immediately after death from the disease, or, more frequently, after death from chloroform

when the animal was dying. These interesting observations are summarized in the following table:—

Animal	Infected on	Infected by	Died on	Duration of disease	Trypanosomes in blood at death	Cerebro-spinal fluid	
						Living tryps.	Cells
1. Dik-dik	23. 9.33	Tsetse bite	6. 3.34	164 days	few	135	8,000
2. "	2.10.33	" "	19.10.33	17 "	numerous	0	3
3. "	21.10.33	" glands	3. 3.34	133 "	few	21	8,000
4. "	26.10.33	" "	25.12.33	55 "	numerous	4	400
5. "	23.11.33	" bite	5. 2.34	74 "	not exam.	0	many
6. "	27.11.33	" "	31.12.33	34 "	numerous	29	many
7. "	22.12.33	" "	22. 3.34	90 "	none	22	678
8. "	21. 1.34	Inoculated from No. 5 Tsetse bite	24. 3.34	62 "	present	6	173
9. Duiker	27. 1.34	Tsetse bite	6. 3.34	38 "	few	5	292

N.B.—Dik-dik 5 died the night before the suboccipital puncture was made.

These animals were caught in a tsetse-free locality and were kept in captivity in a state of good health some months before being infected. Dik-diks and duiker are known to live in tsetse-infected regions, and they are found to frequent farms about dusk. Corson remarks that it is hard to understand how they could survive in sleeping sickness areas unless a combination of relative slight exposure to tsetse bites and habituation to mild strains of *T. brucei* gives them an acquired and selected resistance. It would be interesting to examine the blood of these animals in tsetse-infested regions. W. Y.

REICHENOW (Eduard). Die Züchtung der pathogenen Trypanosomen. [Culture of Pathogenic Trypanosomes.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. July. Vol. 38. No. 7. pp. 292-302. With 6 figs. [12 refs.]

This paper records methods by which *T. gambiense*, *T. congolense* and *T. cruzi* were successfully cultured.

The technique employed was essentially the same as that described in 1929 by the author's pupil, RAZGHA [this *Bulletin*, Vol. 27, p. 244]. The medium consists of citrated human blood and Ringer solution. A series of tapered tubes (centrifuge tubes) containing 1 cc. of Ringer solution, made with 0.6 per cent. sodium chloride, is sterilized, and then to each is added 1 cc. of citrated blood. The medium thus consists of 25 per cent. blood, 25 per cent. sodium citrate solution and 50 per cent. Ringer solution. It is not necessary to deactivate the blood, but it is advantageous to keep the medium 2 or 3 days in the ice chest before use. The optimum temperature for culture is 24°C. and subinoculations should be made every 14 days, although in some cases every 4 weeks suffices.

It is recalled that RAZGHA obtained successful cultures only with recently isolated strains of *T. gambiense*. In his first experiments with *T. gambiense* Reichenow employed the strain "*Gambiense G*," which he formerly had maintained in culture for 111 days. He succeeded in culturing this strain again 1½ years after it was isolated

from man. The cultures were good and were maintained until the 19th passage when they died out. About the same time cultures were made from another strain of *T. gambiense* which was freshly isolated from man. These were also successful and were maintained until the 7th passage when they died out. In an endeavour to explain the reason why the cultures died, the author endeavoured to start new cultures from the same strains, which in the meantime had been maintained in animals. These later attempts were practically failures and it thus became evident that they had lost their cultural capacity. This is not so strange in the case of "*Gambiense G*," which by this time had been isolated from man for $2\frac{1}{2}$ years, but the second strain "*Gambiense Sche*" was only 6 months old. Reichenow, however, observes that the patient had been infected for at least 9 months before the strain was isolated, and he remarks that it has been repeatedly pointed out by DUKE and others that prolonged sojourn of a strain in one vertebrate host may interfere with its capacity to develop in the invertebrate host. The author considers that there is a parallelism between a strain's capacity to be cultured and its power to infect *Glossina*. The cultural forms of *T. gambiense* are described; these are similar to the forms which are seen in the gut of the tsetse fly.

Experiments were next conducted with a 9-year-old strain of *T. congolense*. At first goat's blood was used in the culture medium and the immediate results were excellent, but the first subculture practically failed, only a few tubes exhibiting feeble growths. When, however, human blood was used instead of goat's blood, the cultures were equally good and subcultures were successful. The culture has now been maintained to the 10th passage over a period of 4 months. Reichenow points out that it is strange that human blood is a good culture medium for *T. congolense* in view of the fact that it has a definite therapeutic action in rats infected with this parasite. Again, the culture forms were similar to the developmental forms found in the gut of *Glossina*.

T. cruzi was found to grow better in the blood Ringer medium than in NN-Agar medium, but it was necessary to add a little glucose to the Ringer solution.

W. Y.

PACKCHANIAN (Ardzroony). **Experimental Trypanosoma brucei Infection and Immunity in Various Species of Peromyscus (American Deer Mice).**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 135-147. [18 refs.]

This paper records the pathogenicity of *T. brucei* for a number of species, subspecies and hybrids of American rodents belonging to the genus *Peromyscus*.

The trypanosome used was the strain of nagana sent to England by BRUCE in 1896, and thence to McGill, where it has been maintained ever since in guineapigs. At the time of the experiments it killed guineapigs in 16 to 22 days, and rats and mice within a week.

Peromyscus c. californicus, *P. c. insignis*, *P. c. eremicus*, *P. e. anthonyi* and *P. p. polionotus* all contracted an acute infection and died within 10 days. *P. maniculatus* and its various subspecies exhibited a high resistance to the disease and contracted a subacute infection with

crises and relapses, the duration of the disease being over 80 days. A number of hybrids developed subacute or chronic infections.

W. Y.

FINE (J.). **The Influence of Avitaminosis on the Course of Trypanosome Infection.**—*Jl. Hygiene*. 1934. June. Vol. 34. No. 2. pp. 154-156.

In the experiments recorded here the course of a *T. brucei* infection in rats exhausted of their Vitamin A reserves was compared with that of a similar infection in rats provided with Vitamin A, but otherwise receiving the same diet.

The results of these experiments, which are summarized in a table, show that in both groups trypanosomes appeared in the blood 3 days after inoculation; the average survival for the rats receiving Vitamin A was 9 days, and for those deprived of Vitamin A 8-8 days.

The conclusion reached is that there is no significant difference between the course of *T. brucei* infection in the rat exhausted of Vitamin A and that in the rat adequately supplied with this Vitamin. [It seems to the reviewer that it would be dangerous to generalize from this work that lack of Vitamin A has no influence on trypanosomal infections. It is unfortunate that the author chose such an acute infection. The control animals died so quickly that those deprived of Vitamin A could hardly be expected to die more quickly. It would be interesting to repeat this work with a more chronic infection.]

W. Y.

UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATOLOGÍA REGIONAL ARGENTINA JUJUY. 1934. Publicación No. 16. pp. 3-10. With 3 figs. (1 map); pp. 11-20. With 5 figs. Investigaciones sobre la enfermedad de Chagas. I. Primer caso agudo de la enfermedad de Chagas comprobado en la provincia de Santiago del Estero [RAIMONDI (Silvio) & FEIJOÓ (Enrique J. Canal)]. [The First Acute Case of Chagas's Disease recorded in the Province of Santiago del Estero.] II. Comprobación de formas agudas de la enfermedad de Chagas en Añatuya (Santiago del Estero) [MAZZA (Salvador) & GUERRINI (F. Z.)]. [Acute Forms of Chagas's Disease in Anatuya (Santiago del Estero).]

I. The patient was a boy of 8 years of age, who presented the typical symptoms of this infection in a mild, though acute, form. In his home *Triatoma infestans* was found in large numbers. A map of the Province and district accompanies the article, but is so reduced that with few exceptions the names are illegible even with a lens.

II. Accounts of further cases of this disease in the same Province. The author calls attention to the relative large proportion of patients who die of "syncope"—"the heavy tribute which the inhabitants of the district pay to infection by *Schizotrypanum cruzi*." During the three years 1931-33, out of 233 deaths 22 or 10.6 per cent. died from "cardiac syncope"; the actual figures being, total 79, 72, and 82 respectively, syncope 5, 9, and 8, or 6 and 12 and 9 per cent.

H. H. S.

UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATOLOGÍA REGIONAL ARGENTINA JUJUY. 1934. Publicación No. 17. pp. 3-11. With 3 figs.; pp. 12-16. With 4 figs. pp. 17-23. With 1 fig.; pp. 23-28. With 4 figs.—Investigaciones sobre la enfermedad de Chagas. I. Casos agudos benignos de enfermedad de Chagas comprobados en la provincia de Jujuy [MAZZA (Salvador)]. [**Mild Acute Cases of Chagas's Disease in the Province of Jujuy.**] II. Hallazgo del gato como portador natural del *Schizotrypanum cruzi* en la provincia de Jujuy [MAZZA (Salvador)]. [**The Cat as a Natural Host of Trypanosoma cruzi in the Province of Jujuy.**] III. Comprobación de otra forma aguda de la enfermedad de Chagas en la provincia de Jujuy [MAZZA (Salvador) & ALMARAZ (Pablo)]. [**Another Benign Acute Case of Chagas's Disease in Jujuy.**] IV. Difusión de la infección natural por *Schizotrypanum cruzi* en perros de la provincia de Jujuy [MAZZA (Salvador)]. [**Spread of T. cruzi by Dogs in Jujuy.**]

I & III. The first and third of these papers deal with acute cases of infection by *T. cruzi* but of a comparatively mild character. All those quoted were associated also with malarial infection, usually *P. vivax* or *P. falciparum*. Cases are liable to be overlooked because when examination of the blood has revealed malaria parasites, the diagnosis of paludism is made and investigation of the blood is not pursued further. There is even more excuse for missing the trypanosome infection if the quartan parasite is found for this type of malaria in this district is often associated with oedema of the face and splenomegaly. [Perhaps further study may show that these patients suffer from the dual infection of malaria and trypanosomiasis and that the quartan parasite alone does not so often exhibit its presence by these symptoms.]

II. Previous investigators have examined cats in the dwellings inhabited by patients suffering from *T. cruzi* infection but with negative results as regards the animals harbouring the parasite. The author, however, found a 2-months-old kitten infected and microphotographs show well the presence of the trypanosome "cyst" in the thigh muscles; they were not found elsewhere in the body.

IV. Further proof that dogs, in particular puppies, are carriers of *T. cruzi*. H. H. S.

CHAGAS (Evandro). Atténuation de la virulence du *Trypanosoma cruzi* par son passage dans l'organisme humain. [**Attenuation of the Virulence of T. cruzi by Passage through Man.**]—C. R. Soc. Biol. 1934. Vol. 116. No. 26. p. 1153.

An observation is recorded which, in the author's opinion, indicates that the virulence of *T. cruzi* is attenuated by passage through man.

The strain was obtained from a patient suffering from the chronic cardiac form of the disease. From this patient a guineapig was infected and its blood was then injected into a patient suffering from hopeless cancer. The Machado-Guerreiro reaction (fixation-reaction) was positive on the 10th day and inoculation of the blood into a normal guineapig on the 8th day produced infection. Trypanosomes were found in the peripheral blood only on the 37th day. After 2½ months, the Machado-Guerreiro reaction being still strongly positive and the blood infective for guineapigs, a second cancerous patient

was subinoculated from the first. The result was negative. Apparently the first patient had parasites in his blood because it infected guineapigs, but they were so attenuated that they were unable to produce infection in man. W. Y.

DUNN (Lawrence H.). Attempts to transmit *Trypanosoma cruzi* Chagas with Ticks of the Genus *Ornithodoros*.—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 283-289.

The author has examined experimentally the capacity of *Ornithodoros talaje* and *O. venezuelensis* to transmit *T. cruzi*. Four lots of the former ticks were fed on infected guineapigs, and later on 15 healthy guineapigs; all remained negative. Injection of macerated ticks likewise failed to infect. Several batches of immature and adult *O. venezuelensis* were fed on an infected guineapig and later on healthy animals, but failed to infect; some of the ticks were then macerated and injected into 7 guineapigs, all of which became infected.

From this work it is concluded that neither *O. talaje* nor *O. venezuelensis* commonly transmits *T. cruzi*, but that in the latter species of tick *T. cruzi* may develop and persist for more than six months. W. Y.

DUNN (Lawrence H.). Notes on the Reduviid Bug, *Eratyrus cuspidatus* Stal., naturally infected with *Trypanosoma cruzi* Chagas found in Panama.—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 291-292.

A third species of haematophagous bug of the family Reduviidae has been found in Panama with a natural infection of *T. cruzi*. The bug in question was examined by BARBER at the United States National Museum, who identified it as *Eratyrus cuspidatus* Stal. This species has been found previously only in Columbia and Venezuela. W. Y.

RISQUEZ (Jesús Rafael). Tripanosomosis de los reduviideos de Venezuela. [Infection of Reduviid Bugs by Trypanosomes in Venezuela].—*Gac. Med. de Caracas*. 1934. Apr. 15. Vol. 41. No. 7. pp. 97-100. [20 refs.]

To the author were sent hemiptera from 24 localities in Venezuela; from 20 they arrived in a fit state for examination. Forms of *T. cruzi* have now been found in 8 species of *Triatoma*, viz.: *T. dimidiata*, *T. geniculata*, *T. infestans*, *T. protracta*, *T. rubrofasciata*, *T. sanguisuga*, *T. sordida*, *T. vitticeps*; also in *Rhodnius prolixus* and in *Eratyrus cuspidatus*. In two other species of *Triatoma* [not named] parasites similar to *T. cruzi* have been described and these will very likely prove to be carriers also. H. H. S.

MAZZA (Salvador). Los "gigantocitos quísticos" en los animales experimentalmente infectados con *Trypanosoma cruzi*. ["Cystic Gigantocytes" in Experimental Infections with *T. cruzi*].—*Arch. Ital. Sci. Med. Colon.* 1934. June 1. Vol. 15. No. 6. pp. 403-410. With 3 figs. [17 refs.] English summary (3 lines).

In 1929 MAGARINOS TORRES and PENNA DE AZEVEDO reported finding in the myocardium of the armadillo aggregations of developmental forms of *T. cruzi* within large cells [this *Bulletin*, Vol. 27,

p. 247]. These cells they regarded as the perivascular histiocytes of small arteries. They have now shown that the same may be seen in the myocardium and the thyroid of dogs experimentally inoculated with the faeces of the *Triatoma* vector, or with the blood of human cases of American trypanosomiasis. H. H. S.

NASH (T. A. M.). **The Efficacy of Bush Clearing as a Method of Tsetse Control.**—*West African Med. Jl.* 1934. Apr. Vol. 7. No. 4. pp. 137–139.

Up to date bush clearing remains the only certain method of freeing an area from tsetse fly, and consequently it is a subject of great importance. In this paper the author discusses the various types of clearings now employed.

These are of two kinds, aggressive and defensive :—

(1) *Aggressive Clearings.*—These are directed towards clearing areas by reclaiming a piece of land and rendering it untenable to fly. The tsetse survey made at the end of the dry season often shows that flies which have been menacing a piece of country during the rains have come from a small dry-season concentration area. The removal of this fly sanctuary would greatly reduce the number of tsetse for a considerable distance. The author points out, however, that before steps are taken in this direction, it is important to survey the district thoroughly lest there be alternative sanctuaries available to the fly. Failing better methods of tsetse extermination, aggressive clearing should be our ultimate objective, but at present all available resources must be reserved for the more urgent defensive clearings.

(2) *Defensive Clearings.*—These aim at safeguarding the population during the course of their normal work, or whilst travelling along the main routes. In other words, they aim at reducing the man-fly contact to negligible proportions. Often it is only necessary to clean a strip of vegetation along a river for half a mile in length by 10 yards in width in order to reduce enormously the man-fly contact. It is, of course, essential before embarking on a program of clearing to identify the local tsetse, as the width of clearing depends mainly upon the species and to a lesser extent upon local conditions.

The author considers each of the three common species separately :—

(a) *Glossina palpalis.*—If a fly-infested stream or river passes through cultivation, all heavy forest and thicket must be removed over that part of the stream's course which passes through cultivation, over a distance of a quarter of a mile after the river has entered the surrounding bush. Tall mango trees in the village near the river should be viewed with great distrust and carefully inspected for tsetse during the early dry season, and if fly are found these trees should be cut down or pollarded. It is, of course, essential that the clearings should be constantly cleaned. When a fly-infested river crosses a road, the vegetation should be cleared for a distance of a quarter of a mile on each side of the ford. It is difficult to lay down hard-and-fast rules in the case of *G. palpalis*, but as normally the insect is dependent on heavy shade, small clearings are very efficacious.

(b) *Glossina tachinoides.*—This species is much easier to deal with. Often all that is necessary is to cut down the thin fringe of riverine vegetation which clothes the bank of the local stream; this fringe may be only 10 yards in width and composed of quite small trees.

G. tachinoides never flies far from home, and, consequently, it is unnecessary to extend the clearings of the river banks beyond the limit of cultivation. When *G. tachinoides* infests the main route, all trees should be cut down for a depth of 100 yards on each side of the road, and all small thickets up to a distance of 300 yards.

(c) *G. submorsitans*.—No attempt should be made to clear against this species, unless the matter is very urgent; it is far better to remove the population if possible. *G. submorsitans* will cross the best of clearings, even if it is a mile in width.

The author next discusses the subject of clearing technique, and summarizes his points as follows:—

- " (1) The species of tsetse must first be identified.
- " (2) The clearing must be made early in the dry season.
- " (3) European ring-head axes should be used.
- " (4) The slash should be loosely pulled over the stump, which should first have been packed with grass.
- " (5) The clearing must be protected from fire until late in the dry season, when it should be burnt with a strong following wind.
- " (6) The clearings must be cleaned annually at the end of the rains, and river banks and river beds kept free of all regrowth."

W. Y.

MORRIS (K. R. S.). *The Blonemics and Importance of Glossina longipalpis*, Wied., in the Gold Coast.—*Bull. Entom. Res.* 1934. Sept. Vol. 25. Pt. 3. pp. 309–335. With 11 figs. & 2 maps in text. [15 refs.]

It appears that *Glossina longipalpis* is an important vector of the trypanosomes which attack man* and animals in West Africa. Little or nothing is known of its biology, which is the subject of the present paper.

In the Gold Coast and probably in other areas, the distribution of the insect is limited to "transition forest," and it avoids both the wet equatorial forests and the arid savannah. The author's detailed studies of the insect have been made in a small isolated patch of suitable forest close to Takoradi. In this area he found that the commonest food of the insect is the blood of small antelopes, and that when they were driven out the fly became extremely rare. Indeed, it is evident that the flies which sought human blood are not a fair sample of the wild population, for only a small proportion of the females are pregnant at any time of the year. The author devoted much of his time to a study of climate, and he endeavoured to relate the numbers of flies caught to light, temperature, humidity and rainfall. Within the limited range of conditions which prevailed at Takoradi, it was clear that temperature had a greater effect than the other factors. The author employs correlation coefficients and finds high and significant positive correlation with temperature, and less high but significant correlation with evaporation and sunshine. He observes, moreover, that there is a higher correlation between fly numbers and the temperature of the same week than between fly numbers and the temperature of the previous week; from this one may perhaps conclude that the effect of temperature is rather on the activity of the insects

* The evidence that *longipalpis* is a vector of human trypanosomiasis appears to be slight.—Ed.

themselves than on the size of the *Glossina* population. The author realizes the limitations of his method, and points out that the influence of temperature may be predominant only in the rather uniform climate in which his studies were made; indeed, he is of opinion that in the wider problem of the geographical distribution of the insect, humidity is at least equally important. He finds also that investigating the effect of climatic factors upon the fly is complex not only because the number of factors is great, but also because the flies' activities exhibit a daily rhythm.

It was found that flies in nature were infected with *Trypanosoma gambiense*, *congolense* and *vivax*, and it appears that the fly may become more important in relation to human trypanosomiasis as the agricultural development of the Gold Coast proceeds. It seems that the villager continually shifts his area of cultivation, burning forest and leaving it to regenerate into lower secondary growth which is more suited to this insect. The view is expressed that the native should be encouraged to cultivate a compact area and to keep land in cultivation: this implies the use of manure and of rotation of crops. It seems that if cultivation can be centred round villages and maintained continuously in certain areas, the contact between fly and man will be reduced and the menace of trypanosomiasis lessened.

P. A. Buxton.

LEWIS (D. J.). **The Behaviour of the Larvae of Tsetse-Flies before Pupation.**—*Bull. Entom. Res.* 1934. July. Vol. 25. Pt. 2. pp. 195-199. With 1 plate. [18 refs.]

By comparison with the extremely active larva of the house-fly or the bluebottle, that of a tsetse-fly, which is adapted to an intra-uterine life, is on extrusion a slow-moving creature, which crawls and burrows by means of peristaltic movements and longitudinal contractions, possibly aided in some degree by its soft and tiny antenno-maxillary appendages. It is believed (by SWYNNERTON) that the pregnant female tsetse drops her offspring in haphazard fashion, and is not guided by selective instinct to a patch of suitable ground in which the larva may burrow. Yet the latter, in order to be certain of escaping the attacks of predators and parasites, and securing protection from the fatal results of exposure to the sun, must needs be extruded on to soil in which it can burrow rapidly, and to a sufficient depth. If less fortunate on extrusion, it must crawl until it finds suitable soil in which to burrow.

The observations here described were made at Gadau, in Northern Nigeria, and the species experimented with were *Glossina morsitans*, form *submorsitans* and *G. tachinoides*. When trays respectively filled with wood ash, and with sifted sand of different coarseness, were placed beneath breeding cages containing tsetse-flies, so that the larvae produced fell on to the contents of the trays through coarse wire gauze, it was found that "burrowing efficiency has little or no relation to the weight of the larva." In the case of both species, "more larvae burrowed in coarse than in fine sand, and more in sand than in wood ash." Fine sand with pebbles was readily burrowed into.

A summary is given of statements by previous investigators concerning the burrowing powers of the larvae of various species of *Glossina*, and the nature of the soil in breeding places.

E. E. Austen.

PERLA (David). **The Protective Action of Copper and Iron against *Trypanosoma lewisi* Infection in Albino Rats.**—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 514-520. [13 refs.]

The daily addition of 0.1 mgm. of copper (in the requisite amount of copper sulphate) or 0.1 mgm. of iron (in iron ammonium citrate) or both, to the food of rats for 10 days prior to their intraperitoneal inoculation with blood from a *Trypanosoma lewisi* infected rat will raise the resistance to such an extent that in 50 per cent. of the animals the infection is completely aborted. Lead, when tested in the same way, had no beneficial effect. Young rats brought up on a diet entirely free from copper or iron were not favourable subjects for the development of this trypanosome.

C. M. Wenyon.

SCHWETZ (J.). L'influence de la splénectomie sur l'évolution de *Trypanosoma lewisi*. [**Influence of Splenectomy on the Development of *T. lewisi*.**]—*Bull. Soc. Path. Exot.* 1934. Jan. 10. Vol. 27. No. 1. pp. 62-70

Experimenting with a number of rats the author has found that splenectomy has little if any influence on the course of a *Trypanosoma lewisi* infection. It was not found possible to infect splenectomized mice with this trypanosome.

C. M. W.

GALLIARD (H.). Les formes de multiplication de *Trypanosoma duttoni* Thiroux, au cours d'infections mortelles chez la souris. [**Multiplication Forms of *T. duttoni* in Fatal Infections in Mice.**]—*Ann. Parasit. Humaine et Comparée* 1934. July 1. Vol. 12 No. 4. pp. 273-277. With 2 figs. [13 refs.]

The author has noted that the inoculation of mice already infected with a strain of *Trypanosoma gambiense* of low virulence with the natural mouse trypanosome, *T. duttoni*, may lead to an intense and fatal infection of the latter, during which large numbers of reproducing trypanosomes, like those of *T. lewisi* in the rat, appear in the blood. Normally *T. duttoni* produces a mild infection in mice, which always recover. Conversely the inoculation of mice already infected with *T. duttoni* with the strain of *T. gambiense* leads to an increased virulence of the latter, producing death in 35 to 38 days. Mice infected with the strain of *T. gambiense* alone survived many months.

C. M. W.

LASSABLIÈRE (P.) & PEYCELON (A.). Exaltation de la virulence du *Trypanosoma gambiense*. [**Exaltation of the Virulence of *T. gambiense*.**]—*Rev. Méd. et Hyg. Trop.* 1934. May-June. Vol. 26. No. 3. pp. 138-139.

It is recorded that a strain of *T. gambiense* maintained in guineapigs increased in virulence so as to kill them in 9 to 12 days instead of in 3 or 4 weeks as previously.

W. Y.

REINER (L.) & SMYTHE (C. V.). **Glucose Metabolism of the *Trypanosoma equiperdum* in Vitro.**—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1086-1088.

Experiments were undertaken to estimate the amount of glucose and oxygen consumed by trypanosomes *in vitro* and to ascertain the products formed aerobically and anaerobically. The paper is of a technical nature and should be consulted in the original by those interested.

W. Y.

SCHILLING (Claus), with H. SCHRECK, H. NEUMANN, & H. KUNERT. Versuche zur Schutzimpfung gegen Tsetsekrankheit. I. Teil. [Experiments on Protective Inoculation against Tsetse Diseases.]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Aug. 15. Vol. 83. No. 1/2. pp. 71–94. With 6 figs.

This paper, which apparently was submitted for publication in September, 1933, appears to be very similar to those published after this date in several other journals—English, French and German [this *Bulletin*, Vol. 31, p. 213 and p. 586]. Once more we are given detailed accounts of the foals, "Zeus," "Lottchen" and "Erna"; and these are followed by a theoretical discussion. W. Y.

SCHILLING (S. Claus), assisted by H. SCHRECK, H. NEUMANN & H. KUNERT. Immunisation against Trypanosomiasis.—*East African Med. J.* 1934. June. Vol. 11. No. 3. pp. 83–88.

This paper is substantially the same as one previously published by these authors [this *Bulletin*, Vol. 31, p. 213; p. 586]. W. Y.

NATTAN-LARRIER (L.). Longévité des cultures de *Trypanosoma rabinowitchi*. [Longevity of Cultures of *T. rabinowitchi*.]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 25. pp. 922–924.

The author describes how a culture of *Trypanosoma rabinowitchi* of the hamster on N.N.N. medium prepared with rats' blood was still alive after being kept at 22°C. for 403 days. C. M. W.

KOMIYA (Shoji) & FUJIBAYASHI (Michizo). Beitrag zur Rieckenberg's Reaktion. (Ueber das Trypanolysephänomen.)—*Fukuoka Acta Med. (Fukuoka-Ikwadaigaku-Zasshi)*. 1934. Oct. Vol. 27. No. 10. [In Japanese pp. 2365–2370. German summary p. 124.]

MORODER (Juan). Enfermedad del sueño. Resumen de las publicaciones aparecidas en los últimos cinco años. Prólogo del Prof. Gustavo Pittaluga. —82 pp. [360 refs.]

PARIS EGUILAZ (H.). Contribucion al estudio de los sindromes neurologicos en la trypanosomiasis humana.—*Medicina Paises Calidos*. Madrid. 1934. Aug. Vol. 7. No. 8. pp. 362–369.

STEUDEL (E.). Wie bewährt sich Bayer 205 als Heilmittel gegen die Schlafkrankheit? Nachtrag zu dem gleichnamigen Artikel in Nr. 51, S.2009, Jahrg. 1933 ds. Wschr.—*Muench. Med. Woch.* 1934. Aug. 10. Vol. 81. No. 32. pp. 1235–1236.

TORREALBA (J. F.). Algo mas sobre tripanosomosis ensayos de xenodiagnostico. —*Gac. Med. de Caracas*. 1934. Feb. 15. Vol. 41. No. 3. pp. 33–37.

UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATOLOGÍA REGIONAL ARGENTINA JUJUY. 1934. Publicación No. 15. pp. 1–24. With 15 figs. [21 refs.] Investigaciones sobre la enfermedad de Chagas. I. Sobre nódulos de histiocitosis en el Hígado de perro inoculado con *Schizotrypanum cruzi* Chagas, de origen humano [MAZZA (Salvador) & JORG (M.E.)].

UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATOLOGÍA REGIONAL ARGENTINA JUJUY. 1934. Publicación No. 15. pp. 25–54. With 1 chart & 33 figs. Investigaciones sobre la enfermedad de Chagas. II. Otro caso de forma aguda de enfermedad de Chagas observado en el norte santafecino [MAZZA (Salvador) & ROMAÑA (Cecilio)].

SPRUE.

MACKIE (Thomas T.). **Nontropical Sprue.**—Reprinted from *Med. Clinics North America*. 1933. Vol. 17. pp. 165–184. With 2 figs. [61 refs.]

This article, though entitled Non-tropical Sprue, starts by giving an excellent and well-balanced account of the condition as it occurs in tropical countries and is one of the best short summaries of our present state of knowledge the reviewer has read for a long time. Due credit is given to all those who have made a name in this field of research; their views are stated fairly and criticized without bias.

In the latter half of the article the author details a case presenting all the characteristic features of sprue, the patient, a woman of 43 years, having lived practically all her life in New Jersey, and never having visited a country where sprue is endemic. There is no need here to describe in detail the symptoms; the case was obviously one of severe grade and all the usual modes of treatment were adopted. It affords another example of the value of intensive liver therapy, administered parenterally, and at the same time shows that intravenously it may induce a rapid fall in blood values.

The article ends with a very good bibliography, the only omission of note being reference to the larger work, the book by Professor THAYSEN on this subject (see this *Bulletin*, Vol. 30, p. 57). Smaller papers by the same author are mentioned. This book perhaps has not come to Dr. Mackie's notice for in his list of cases of non-tropical sprue, which he regards as comprehensive, there are some not given which are mentioned in Professor THAYSEN'S work, *e.g.*, some of the cases recorded in Norway, Denmark, Germany and Switzerland. Dr. Mackie and his collaborator, Miss HENRIQUES, have done good service in putting this vexed subject so clearly and succinctly before us.

H. H. S.

THORFINN (Einar). **A Contribution to the Knowledge of Native Sprue in Sweden.**—*Acta Med. Scandinavica*. 1933. Vol. 80. No. 4–6. pp. 389–402. With 2 figs.

The case detailed in this article is the third indigenous in Sweden, possibly the fourth but there was a little doubt concerning one recorded by ENGEL in 1931.

The present patient was a woman of 36 years who had exhibited certain sprue-like symptoms on and off for 10 years. The clinical condition need not be detailed, for it was very typical—languor, debility, dry wrinkled skin, loss of weight, some anaemia, low blood pressure, low blood calcium, copious, frothy grey stools; the tongue was not affected till later. Results of physical and laboratory examinations are stated [enumeration of tests by mere names is to be deprecated; thus very little information is conveyed by the statements: urine Schlesinger negative; faeces Schlesinger highly positive, Weber negative, Schmidt positive].

Interest lies in the facts that blood transfusion was needed, and that diet and the administration of calcium were practically ineffectual till tabloids of parathyroid were also given. The patient left hospital much improved; she had gained 2.2 kgm. in weight, the stools were solid, but still contained more than the normal amount of fat. A

month later a relapse began and she was again admitted to hospital where she remained for nearly 8 weeks; she was treated by hydrochloric acid, calcium and vigantol and a diet "rich in protein and carbohydrate and with as little fat as possible." Improvement was less marked than on the first occasion and when seen two months later the stools were still light in colour, occasionally loose and there had been some stomatitis, but there had been a slight increase in weight and "the general condition was rather good." No parathyroid was given on the second admission to hospital and the diet "rich in carbohydrate" is against the most modern treatment. [The references given are all Scandinavian; no mention is made of the work of FAIRLEY and others in Great Britain.] H. H. S.

MILLER (Reginald). **Sprue commencing at 11½ Years of Age.**—*Proc. Roy. Soc. Med.* 1933. Dec. Vol. 27. No. 2. pp. 113-115 (Sect. for Study of Dis. in Children pp. 1-3). Also in *Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. pp. 413-416.

The most noteworthy feature of the case here recorded is the age of the patient. Generally speaking sprue is a disease of adults; though instances of adolescents are recorded they are very uncommon, and, so far as the reviewer is aware, none have been reported so young as this, 11½ years. Apart from this, the case—the history, clinical condition, response to treatment—is a typical one. The child lived from the age of 5 to 11 years in Ceylon, developed gastro-intestinal symptoms six months after returning to England and stomatitis six months later. There were wasting, fatty, copious, pale stools and anaemia (r.b.c. 1,400,000; Hb. 36 per cent., C.I. 1.3) of megalocytic type (8-8.5 μ). Treatment with high protein, low fat and low carbohydrate diet and liver extract led, as usual, to marked improvement.

H. H. S.

LOW (G. Carmichael) & FAIRLEY (N. Hamilton). **Fatal Perforation of the Caecum in a Case of Sprue.**—*Brit. Med. J.* 1934. Oct. 13. pp. 678-679. With 1 chart.

Perforation of a sprue lesion in the large intestine must be of rare occurrence. All the previous records in the literature to which the authors refer were of perforations of ulcers in the small intestine.

The patient, a woman of 58 years, had lived for a quarter of a century in India and during the first 2 years of her residence there had suffered from malaria and dysentery. Sprue symptoms first made their appearance in the last year of her stay in India; these symptoms were typical, together with considerable anaemia of the megalocytic type—r.b.c. 1,700,000 per cmm., Hb. 50 per cent., C.I. 1.4, average corpuscle diameter 8.6 μ . Serum calcium was down to 8.7 mgm. per 100 cc. On a treatment with high protein, low fat and carbohydrate she made considerable progress. In 6½ weeks the r.b.c. were 3,585,000 per cmm., Hb. 50 per cent., C.I. 0.7. Two days later signs of perforation and peritonitis appeared suddenly, and at operation the site of the perforation was found "posteriorly, . . . at the junction of a mobile caecum and ascending colon some two-and-a-half inches above the base of the appendix." The patient died. H. H. S.

MACKIE (F. P.) & FAIRLEY (N. Hamilton). **Gross and Microscopic Anatomy of the Intestinal Canal from Two Cases of Sprue.** [Laboratory Meeting Demonstration.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. p. 340.

The two specimens of intestine from sprue patients shown at the Clinical Laboratory meeting of the Royal Society of Tropical Medicine and Hygiene in November 1933 are of more than ordinary interest. In the first place the autopsy was performed so soon after death that post-mortem changes can be excluded. In the second place the hitherto recognized idea that an essential part of the morbid anatomy of this disease is a thinning of the bowel "to such an extent as to be almost diaphanous" is shown not to hold good for all cases and since examination rarely (if ever before) has been made so early after death, we are led to wonder whether this is not in great degree, perhaps entirely, a post-mortem change, for in neither of those exhibited on this occasion was any thinning found, or any other macroscopic morbid change except congestion of the margins of the valvulae conniventes. Moreover, microscopical examination also revealed no change of importance.

H. H. S.

RHOADS (C. P.) & CASTLE (W. B.). **The Pathology of the Bone Marrow in Sprue Anemia.**—*Amer. Jl. Path.* 1933. Vol. 9. No. 54. Supp. pp. 813-826. With 6 figs. on 3 plates. [13 refs.]

Describes the marrow changes occurring in sprue and suggests an explanation of the variations in results previously recorded.

The somewhat divergent results of examinations of bone marrow in sprue, as recorded by MACKIE & FAIRLEY, KRJUKOFF, ASHFORD, and others, are ascribable to two chief causes: first, some specimens were taken in life, others after death; second, the specimens studied were not always from comparable sites. The sternal marrow may reveal changes when that of the long bones shows none.

This article is based almost entirely on specimens of marrow from the sternum (in three from the femur also). Twenty-two patients were studied; sixteen were untreated cases, five treated, and in three the examinations were made after death. In some the samples were taken both before and after a remission and in others during the height of reticulocyte response to liver therapy. The results are presented fully in tabular form; this table should be studied in detail. A few remarks may here be made on illustrative cases.

1. A Porto Rican woman of 47 years, with typical sprue of one year's duration. The bone marrow was moderately cellular and treatment with liver extract even in large doses led neither to reticulocyte rise nor to improvement in the blood. Both, however, were satisfactorily accomplished when iron (Ferri et ammon. cit.) was given.

2. A man of 60 years, with sprue symptoms for ten years. Before the specimen of marrow was taken he was given Ferri et ammon. cit. 6 gm. daily for 10 days without effect. Liver extract *per os* was followed by a slight rise in reticulocytes but the normal was not attained till after parenteral administration.

3. A Porto Rican woman of 60 years; sprue symptoms for a year. The marrow showed diffuse megaloblastic hyperplasia, similar to that of pernicious anaemia. Restoration to normal resulted from intramuscular injection of liver extract.

In two instances sternal puncture was performed at different stages and the histological pictures compared. One case is presented in detail together with photomicrographs to illustrate the differences, which are very considerable. The effect of the liver treatment was to bring about a maturation of megaloblasts to normoblasts and produce a bone marrow approaching the normal and resembling the transition observed in pernicious anaemia in course of treatment.

The post-mortem specimens resembled those found in patients dying of pernicious anaemia; large marrow cells contained erythrocytes, the cells varied much in size and shape, some being very large and irregular with basophilic cytoplasm and containing many red corpuscles. Since this phagocytosis of erythrocytes was observed in post-mortem specimens only, the authors conclude that it is a post-mortem change.

They find that the alterations accompanying the anaemia of sprue are similar to those of pernicious anaemia; that the anaemia of relapse results from the inability of the megaloblasts to form mature red corpuscles. The same fundamental change was observed in all the untreated cases—increase in number and size of megaloblasts, decrease in the fat, in number of megakaryocytes and cells of the granulocytic series. These changes found in sternal marrow may not be present in that of the long bones. During relapse the essential changes are proliferation of megaloblasts and reduction, even suppression, of maturation to the normoblast stage, restoration occurring when clinical remission takes place. [An article important for all engaged in pathological research on sprue. The photographs are well reproduced, but uncoloured they do not convey much information except when the differences are marked as in Figs. 4 and 5 depicting the marrow taken at different times from the same patient.] H. H. S.

BLANC (F.) & BORDES (L. A.). A propos du traitement de la sprue. [The Treatment of Sprue].—*Marseille-Méd.* 1934. Feb. 25. Vol. 71. No. 6. pp. 297-301.

The authors' views are that, granting that the pathogeny of sprue is not yet fully clear, "we can at least explain the various symptoms of sprue as arising from a primary functional disturbance—a defect in the functions of the intestinal mucosa."

Their treatment consists in giving such form of nourishment as can be absorbed by a defective mucous membrane, namely the different sugars, hexoses and pentoses, glucose, laevulose, arabinose, in the form of fruit cooked or raw; in addition raw meat (beef, mutton and horseflesh "whose absorption is facilitated by pepsin powder"). Further they give daily a shot-gun endocrine prescription containing pepsin, pancreatin, thyroid extract, insulin and adrenalin. Though they have not met with calcium deficiency "nevertheless we give calcium salts." Some patients, they state, take raw calves' liver with difficulty! No cases are detailed and no comment is needed.

H. H. S.

RHOADS (C. P.) & MILLER (D. K.). **Intensive Liver Extract Therapy of Sprue.**—*Jl. Amer. Med. Assoc.* 1934. Aug. 11. Vol. 103. No. 6. pp. 387-391. With 4 charts. [14 refs.]

Examination of the various forms of dietetic treatment which have from time to time been recommended for and found successful in sprue has convinced the authors that the single factor common to all is a relatively high content of water-soluble vitamins. From this it is argued first that a lack of this vitamin exists in certain cases of the disease and, second, that this lack is "perhaps causal." [Neither of these points is anyone who has studied this disease likely to dispute.] The authors also state that "sprue may result from surgical intervention with the absorbing surface of the bowel." It is true that certain sprue-like symptoms may result from interference with absorption, but one would like more confirmation that surgical sprue exists.

Four cases are related briefly, patients who had not reacted effectively to ordinary modes of treatment, but improved greatly after intensive liver treatment administered parenterally—intramuscular injections of extract-Lilly, or the Parke, Davis & Co.'s preparation for intravenous use. [No reference is made to the large amount of research on sprue carried out by English workers in recent years.]

H. H. S.

RIEDER (Wilhelm). Erfahrungen bei der Behandlung einer Sprue-Tetanie mit A.T. 10. [Treatment of Sprue Tetany with A.T. 10.]—*Muench. Med. Woch.* 1934. Oct. 19. Vol. 81. No. 42. pp. 1610-1611. With 1 fig.

A.T. 10 is a preparation by Holtz, and was recommended by the author last year as the treatment for post-operative tetany. [Its composition is not stated.] He has now tried it in a case of sprue of long standing with excellent result after failure of other measures.

The patient had been under treatment of one kind or another almost uninterruptedly since 1919, and finally in 1932 came under the care of Professor GRIESBACH in Hamburg. With pancreon and parathormone he improved for a time, and the same results succeeded the administration of parathyroid. In January, 1934, he complained of lassitude, incapacity for work, and cramps in the hands and feet with tetany, as observed by the author to whose care the patient had been transferred, and stools of a fatty, sprue-like character numbered 15-20 a day. Blood pressure was low 100/65; calcium 4.8 mgm. per cent. (it had been as low as 3.5 in 1932). A.T. 10 was given [dose not stated here, but in later treatment it was given in doses of "2.5-3 cc. average"] and in a fortnight the blood calcium rose to 9.7 mgm. and in 4 weeks the stools were reduced to 5 a day. At the end of March, after another week's treatment with A.T. 10, the calcium was 10.5 mgm. per cent., but the number of stools did not diminish further. From the middle of April the drug was continued but in combination with raw apples, 8-10 daily, and the stools were reduced to one or at most two daily. Since then [the paper is not dated but the graph continues to June when presumably he left hospital to resume work] he has remained well, "feels himself equal to any demand that his occupation [not mentioned] makes upon him and states that he is the happiest man in the world."

H. H. S.

THAYSEN (Th. E. Hess). To Tilfælde af idiopatisk Steatorré. Med særligt Henblik paa Diagnosen og Forekomsten af Symptomer paa Endocripathi og Avitaminose. [**Two Cases of Idiopathic Steatorrhoea. Were the Symptoms due to Endocrine Disease or to an Avitaminosis?**—*Hospitalstidende*. 1934. Sept. 25. Vol. 77. No. 39. pp. 1033–1052. With 8 figs. (2 coloured on plate.)

Several papers have been published in Denmark on idiopathic steatorrhoea, and all have appeared in the period 1924–32. Evidently it is not very rare, and it is the more important for being readily overlooked and given some misleading label. The histories of Hess Thaysen's two patients (a man of 32 and a woman of 24) have this, among many other things, in common that they spent years in receiving hospital treatment as varied as the mistaken diagnoses. In the man's case, some of these diagnoses were gastric achylia, severe simple anaemia, haemolytic anaemia, chronic diarrhoea, pleuritis, tuberculous enteritis, renal tuberculosis, tuberculous epididymitis, tuberculous adenitis, heart disease, pulmonary tuberculosis, hypoadrenalism, megacolon, Addison's disease, and pluri-glandular insufficiency. The list of previous diagnoses in the woman's case was almost equally long and varied, and it included infantilism. It may be noted that in both cases Addison's disease was diagnosed on the strength of pigmentation. Since early childhood the second patient had been subject to periodic attacks of diarrhoea, with bulky, thin, foul, whitish or grey stools. Her build was definitely infantile, and she had a distended abdomen, though she was in other respects lean. Simple anaemia, glossitis, a low blood-sugar curve, increased basal metabolism, osteoporosis and latent tetany were observed in her case. After discussing the alternative diagnoses of endocrine disease and vitamin deficiency, and pointing out how many of the patients' symptoms could be correlated with one or other of these conditions, the author comes back to the problem of diagnosis. During one or more of their many stays in hospital, these patients must have passed the stools characteristic of steatorrhoea. It was, presumably, overlooked because of the quasi-universal hospital practice of consigning to nurses the duty of inspecting and passing judgment on stools. [See this *Bulletin*, Vol. 30, p. 57.]

C. Lillingston.

DÜNNER (L.), HIRSCHFELD (H.) & GERALDY (M.). Zur Pathogenese und Klinik der nichttropischen Sprue (Fettresorptionskrankheit).—*Klin. Woch.* 1934. Jan. 27. Vol. 13. No. 4. pp. 138–141. With 1 fig.

SNIJDEERS (E. P.). Over Tropische spruw.—*Nederl. Tijdschr. v. Geneesk.* 1934. Sept. 22. Vol. 78. No. 38. pp. 4276–4285. With 6 figs. (3 on 1 plate).

VAN DEN BERGH (A. A. Hijmans). Een op spruw gelijkend ziektebeeld.—*Nederl. Tijdschr. v. Geneesk.* 1934. June 9. Vol. 78. No. 23. pp. 2559–2564.

YAWS AND SYPHILIS.

TURNER (Thomas B.), SAUNDERS (George M.) & JOHNSTON (H. M.), Jr.
Report of the Jamaica Yaws Commission for 1932.—28 pp. With
 66 figs. on 14 plates & 12 charts. 1934. Kingston: Govt.
 Printing Office.

At the request of the Government of Jamaica, the International Health Division of the Rockefeller Foundation agreed to undertake, on a co-operative basis, an investigation of yaws in the hope of devising more effective means of control. Thereupon the Jamaica Yaws Commission was organized and began to function in January 1932.

The present report is the result of the first year's work, and includes some general considerations upon the area selected for study, the method of survey to be carried out and some preliminary clinical observations based upon the first 1,500 cases admitted to the clinic. It may be stated at once that there is little essentially new to record but the observations of the commission are useful as confirmatory evidence upon certain points. The 1,500 cases studied comprised :—

	Per cent.
Yaws	917 or 61·1
Probably syphilis	15 „ 1·0
No history : positive serology	113 „ 7·5
No history : equivocal serology	30 „ 2·0
No history : negative serology	425 „ 28·3 [not 38·3]

91 per cent. of infections were acquired before the age of 15.

The primary yaw only differs slightly from the generalized yaw in appearance but tends to be larger. Many primary lesions are probably so insignificant as to escape notice. Enlargement of regional lymphatic glands is constant. *Sp. pertenuis* was demonstrated in the regional lymph nodes in two instances [it is not stated whether these were the only attempts made or not ; it would have been of value if similar examinations had been carried out in a large series]. "It would appear that dissemination of the organism by way of the lymphatics occurs before, and possibly as a necessary prelude to, the bloodstream dissemination which takes place eventually" [evidence on this point is sorely needed, the above statement would appear to rest on the findings in a single case]. "Despite the wide dissemination of virus which must occur, recognizable pathological changes are not often induced in any tissue save the skin and the bones." Among the 1,500 patients were eight presenting various [but undescribed] neurological lesions and with one exception a history of past yaws. The spinal fluid was definitely positive in 2, equivocal in 4 and negative in 2. The report states "The available evidence indicates that yaws probably gives rise to neurological disease in rare instances although it is desirable to have observations on a larger number of patients before making a final appraisal of the question." [It is certainly to be hoped that opportunity will arise of obtaining proof one way or the other and that "probables" will be discarded.] The evidence so far obtained in regard to cardiovascular lesions is of the same order.

A finding which must have considerable interest is stated thus :—

"Three patients presented lesions of the testis or epididymis which can be ascribed to yaws.

"Case 16.—Aged 9 years ; duration of infection 18 months, one previous treatment. Numerous skin lesions of the 'late' type. Left testis twice size of right, lower half occupied by hard nodule.

"Case 563.—Aged 5 years ; duration of infection 1 month ; multiple dark-field positive framboesiform lesions and multiple bone lesions. Left testis enlarged, firm, irregular, painless.

"Case 1176.—Aged 2 years ; duration of infection 1 month, primary and generalized skin lesions dark-field positive. Multiple bone lesions, right testis enlarged to twice its normal size, firm, irregular, painless. In the epididymis were several small nodules strikingly like those which occur in the rabbit's epididymis in experimental yaws."

[From these notes it is doubtful what is meant by the phrase above given "which can be ascribed to yaws." Will they be *proved* to be definitely due to yaws and not merely left as cases of testicular enlargements in yaws subjects?] "No instance of iritis or keratitis has been seen." "No lesion of the liver attributable to yaws was observed." All the well-known framboesial affections of the skin have been noted including plantar and palmar affections. "Involvement of mucous membranes alone in yaws is exceedingly rare . . . Papules lying wholly upon the mucous membrane surface . . . suggest direct inoculation." No true lesions of mucous membranes were seen.

The common well-known bone and joint lesions were met with, as in yaws elsewhere, in from 15-20 per cent. Several attempts to demonstrate the spirochaete in material obtained from bone lesions failed. The frequency of bone lesions demonstrable by X-ray was : tibia 39 : fibula 16 : ulna 18 : radius 14 : humerus 13 : femur 5 : carpal and metacarpal 14 : tarsal and metatarsal 3 : skull 2 : nose 3 : patella 1. Total cases 65. [Information is wanted upon the pathological changes in bone, the histological picture and the distribution of the organisms.] Seven patients presented characteristic juxta-articular nodules. All gave positive W.R. No history of yaws in three and a differential diagnosis could not be made. Two cases of goundou were seen—one a girl aged 12 with yaws of 9 years' duration, and multiple bone and late skin lesions, the other a man of 67 with yaws of about 60 years' duration, positive W.R. but no other lesions. Gangosa not infrequent but only one case admitted to the clinic. It was noted that "among our entire group of patients with generalized skin lesions there has not been one in which the rash, when viewed as a whole, would be confused by a qualified observer with that of syphilis."

Some of the results in attempts to evaluate treatment are as follows : The serological reaction in over 50 per cent. of cases treated by six injections of some one of the well-tried drugs is positive when tested 6-9 months after treatment. Lesions heal most readily after treatment with neo-arsphenamine but this arsenical is followed with just as bad a serological relapse rate as any other. With halarsol results are uncertain—further investigation is necessary. With bismuth preparations persisting infections are commoner than with the arsenical. Neo-bismuth preparations offer better results. Carbarsone deserves further trial.

No pathological work nor animal experimental research has yet been carried out. [The histo-pathological changes in yaws certainly need study afresh.]

Finally, the authors of the Report say "Whatever was the relation of yaws and syphilis one century or four centuries ago, it can be said

that at the present time the two diseases are not identical. . . . Advantage should be taken of the opportunity to study the two diseases concurrently."

[May we hope this Commission will do so. All those interested in the problem await "a sign from heaven," some acid test in differential diagnosis.] *H. S. Stannus.*

PURCELL (F. W.). **Aetiology of Yaws.**—*West African Med. Jl.* 1933. Oct. Vol. 7. No. 2. pp. 96-97.

In this article the author relates his observations upon some 5,000 cases of yaws, treated in 1928, among a single isolated tribe—the Konkomba—of the Eastern Dagomba District of the Northern Territories of the Gold Coast. They are offered as a contribution to the aetiology of the yaws-syphilis problem.

The Konkomba are an aloof people who do not marry into other tribes nor have other relations with them. No venereally contracted diseases, including gonorrhoea, occur among these people. Syphilis, acquired or congenital, as ordinarily diagnosed clinically is never seen. On the other hand a large proportion become infected with yaws, generally in childhood, among the uncleanly more especially. Reinfection, it is stated, may occur. The primary lesion in children is usually found on areas of skin exposed to contamination with the ground or exposed to injury by the finger-nails—the anus, the prepuce, the corners of the mouth and eye, etc.

The author is unable to entertain the idea that "yaws is epidemic non-venereal syphilis transmitted innocently among primitive people."

H. S. S.

BURKE (H. L.). **Some Notes on the Aetiology, Symptomatology and Treatment of Yaws in North-Eastern Adamawa Province, Nigeria.**—*West African Med. Jl.* 1933. Oct. Vol. 7. No. 2. pp. 94-96.

A study of 580 cases of yaws from the north-eastern portion of Adamawa Province of Nigeria and the adjacent area of British Cameroons, at the Lassa Hospital of the Church of the Brethren Mission.

It is noted that the Moslem population (Fulani) had no word for yaws while the pagan tribes had no word for syphilis, yaws being very rare among the Fulani and syphilis equally exceptional among the pagan peoples. [Illustrating again the well-known fact that yaws tends to be a disease of the less civilized who live in the bush while syphilis tends to occur among the more civilized living in communities.] "With a little experience the difference between yaws and syphilis is quite apparent."

Cases of primary yaws (36) seldom seek treatment; the majority of the sick (347) were in the stage of generalized eruption. The tertiary cases (101) most commonly presented lesions of the palms of the hands and soles of the feet, which had appeared 12-15 years after infection. Tibial periostitis, "prepatellar bursitis," "nodules of the sternum," "deformations of the skull," and gangosa are mentioned but there is no reference to the occurrence of juxta-articular nodules or goundou.

H. S. S.

WILSON (Paul W.). **Atypical Yaws.**—*Amer. Jl. Trop. Med.* 1934. Jan. Vol. 14. No. 1. pp. 1–25. With 19 figs.

A description of what are considered by the author to be atypical lesions met with during a study of 424 consecutive cases of yaws in Panama. A comparison is made between these cases and those of a series of 1,423 cases reported from Haiti. [See this *Bulletin*, Vol. 27, p. 708.]

Notes of twenty cases are given and the following conclusions drawn :—

" 1. The yaws cases seen in Panama show a marked tendency to local and regional limitation of late pathology [lesions].

" 2. Compared with yaws in Haiti, this regional limitation in the Panama series is double that found among the Haitien cases.

" 3. The route of transmission of infection from the primary yaw to other parts of the skin surface cannot be definitely traced in many instances but considerable evidence indicates an impetigo-like spread, *i.e.*, a mechanical transfer of infectious material over the body surface.

" 4. Undoubtedly transfer of the infection within the body is accomplished through the lymphatic system or general circulation in a small percentage of cases.

" 5. With but two exceptions all periosteal cases in the Panama group were caused by direct extension of the infection from overlying ulcers.

" 6. The strain of *T. pertenue* found in Panama is a much less virulent strain than that encountered in Haiti.

" 7. 'Dry yaws' eruption, either of the ringworm or non-progressive papular type, probably accounts for the long quiescent periods so frequently seen in cases of late yaws.

" 8. 'Dry yaws' on the skin around joint protuberances probably indicates the portal of infection which later manifests itself as a juxta articular node

" 9. It is believed that very rarely yaws may be the *accidental* etiological factor in aneurysm and cerebral thrombosis or cerebral hemorrhage of young adults."

H. S. S.

HEWER (T. F.). **Some Observations on Yaws and Syphilis in the Southern Sudan.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. May 9. Vol. 27. No. 6. pp. 593–608. With 4 figs. on 1 plate.

The author had hoped to be able to make a comparative study of parallel series of cases of yaws and syphilis. His paper deals with observations made upon 250 cases of yaws and syphilis studied clinically and 1,000 others seen casually. He found himself unable to do more than place some proportion of his cases in one or other category of probably yaws or probably syphilis.

Many of the observations are very interesting though their value is uncertain as is always the case when they are correlated with histories depending on native information. As an example "a history of a primary on the genitals" can have little value without knowing definitely whether the primary was indeed a primary and then whether it was a primary syphilitic chancre or a primary yaw.

The reference to lesions on the mucous membranes are particularly interesting. Among 256 cases there are 62 with some lesion of the mucous membrane of the mouth or throat, of which 35 gave a history of sore throat and 21 of hoarseness in the early secondary stage; 29 had mucous patches just inside the lips, 7 inside the cheeks. Of the 62 in

14 there was a history of a primary lesion on the genitals, 35 of an extra genital lesion, 13 were doubtful. Some of these had typical framboesia and crab yaws, many had genital condylomata and often no other manifestation. The author does not specifically aver that mucous patches occur in yaws but the inference is made and he offers as an explanation of this possibility the fact that the whole population chews tobacco and infants are given plugs of tobacco already chewed by their mothers.

No visceral lesions were discovered save a single case of aortic regurgitation attributable to syphilis.

In 246 cases the cerebrospinal fluid was examined, the standard of normality adopted being 3 cells and under, an upper limit of 30 mgm. total protein and negative Pandy test. The cases were divided into probably yaws, probably syphilis, and doubtful, and these again into three groups according to the duration of the disease. The yaws cases numbered 44 and among these "definite abnormalities were found" in five. It is worth noting, however, that the cell counts were $3\frac{1}{2}$, 7, $3\frac{1}{2}$, $6\frac{1}{2}$, $\frac{1}{2}$, figures which many syphilologists would pass as normal, the ranges in total protein 55, 30, 25, 20 and 50 mgm. per cent. The Pandy reaction was only done in two cases and in both it was positive. The author says, "in none of these cases was the change a gross one." In view of their numbers and lack of any series of controls and the fact that such changes are in no sense specific it seems questionable how they should be interpreted. It is a pity no W.R. were done on these fluids. No case of involvement of the nervous system was diagnosed clinically.

The facts given in regard to congenital transmission based on native evidence are too few and too uncertain to have much value.

H. S. S.

LE SCOUÉZEC. Syphilis avec réactions méningées et pian chez les indigènes du Camérout. [**Syphilis with Meningeal Reactions and Yaws in Cameroon Natives.**]—*Arch. Inst. Prophylactique*. 1934. Apr.-June. Vol. 6. No. 2. pp. 186-190. English summary pp. 189-190.

The results of examination of the cerebrospinal fluid from cases of syphilis and yaws among natives of French Cameroon.

Of 3,045 fluids from syphilitics 1,412 or 46.37 per cent. were absolutely normal; 1,633 or 53.63 showed a more or less pathological deviation from normal using (1) Vernes-perethynol test, (2) hyperleucocytosis, (3) hyperalbuminosis as criteria. 7.6 per cent. showed (1)+(2)+(3); 22.9 per cent. (2)+(3); 23.7 per cent. (2) only; 45.8 per cent. (3) only.

The blood of 74 natives suffering from florid yaws, with the exception of two, showed sero-flocculation with Vernes-pyretlynol test. The C.S.F. of these 74 cases was normal except in 2 cases both of which showed positive flocculation (1) associated with (2)+(3); there were 9 in which (2) alone and 11 in which (3) alone was encountered.

Some of these fluids might be considered within the limits of normal by other observers and though these yaws cases showed no sign of syphilis and denied syphilis the author, very rightly, says he would not like to assert that these changes in the C.S.F. of yaws cases are due to yaws.

H. S. S.

MONTEL (M. L. R.), MASSARI (P.) & LE-VAN-PHUNG. Un cas de pian osseux tertiaire. [**Case of Tertiary Yaws : Bone Changes.**]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. May. Vol. 12. No. 5. pp. 477-482. With 4 figs.

A description of tertiary bony lesions with radiographic findings in a 15 year old Annamese boy.

The clinical picture calls for no special mention but the lesions shown by X-ray examination are worthy of note. They resembled those previously described by other authors and appear to have specific characteristics :—multiple and localized thickenings of the bones more especially the long bones, both epiphysis and diaphysis, the periosteum and bone both being involved, with obliteration of the medullary canal but preservation of the trabecular arrangement of the bony tissue. In these zones of thickening numerous rounded areas of rarefaction varying in size are seen always surrounded by a zone of more marked condensation. These areas of rarefaction sometimes involve the border of a bone and give rise to an appearance as if a piece of the bone had been bitten out. Between the areas of thickening a certain amount of decalcification may be seen.

In syphilis the lesions are less irregular, less numerous, and the medullary canal persists though with some degree of narrowing. In yaws the lesions in some ways rather resemble those seen in fibro-cystic disease of bone.

H. S. S.

FITZGERALD (G. H.) & GUPTA (Prafulla Kumar Das). **The Treatment of Yaws.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. pp. 371-384. [15 refs.]

An attempt to evaluate various methods of treatment in yaws. Local conditions in Assam demanded a method which was cheap, painless and free from danger and which could be administered by the needle.

The best results were obtained, the authors consider, with 2 or 3 injections of neosalvarsan (0.01 gm. per kg. body weight) combined with 8 injections of bismuth (1.5 gm. bismuth metal). Serological cure was obtained in half the cases and freedom from clinical relapse in all but 5 per cent. This course involved 8 weekly attendances and was possible in the area under observation but one which might not be possible in other yaws districts.

Neosalvarsan or one of its substitutes alone failed ; 80 per cent. of cases treated by 1 to 3 injections were either clinically or serologically positive two years after treatment.

A number of bismuth preparations were tried out ; that which appeared to have greatest advantages was "Casbis." Given alone like other bismuth salts, it was of little value in effecting persistently good results but in combination with the arsenical as above mentioned it was the most useful.

Halarsol has practically no value alone ; combined with bismuth it is more effective. Notes of trials with other drugs are given but in no case were useful results obtained.

H. S. S.

OCCHINO (A) & KERNKAMP (Y.). Le traitement de quelques affections et notamment du pian par les injections intraveineuses de sulfate de cuivre. [**Treatment of Yaws by Intravenous Injections of Copper Sulphate.**—*Ann. Soc. Belge de Méd. Trop.* 1933. Dec. 31. Vol. 13. No. 4. pp. 397-404. With 8 figs.

A short paper upon the uses of intravenous copper sulphate therapy in yaws and some other conditions, including impetigo, erysipelas and leprosy.

Secondary yaws cases to a total of 209 were selected for trial. The course of treatment consisted in the daily intravenous injection of a 6 per mille aqueous solution of copper sulphate ($\text{Cu SO}_4 \cdot 5 \text{ H}_2\text{O}$) in 10 cc. doses for adults and half that amount for children of 10 years of age. "Blanchissement" was obtained in from 10 to 25 days. A further 5 injections were given as "a treatment of consolidation." No relapse occurred in 193 of these cases which remained under observation for from 2 to 5 months.

These results the authors hold are comparable with those obtained with arsenic and bismuth. The one disadvantage is that the method entails *daily* treatment. The advantages are the ease of preparation, absence of unpleasant reactions and very low costs. Relief of pain is obtained early. [No serological reactions were carried out and with an observation period of only 2 to 5 months it is obviously uncertain how this form of treatment should be evaluated in regard to cure of the infection.] H. S. S.

BAIS (W. J.). Ueber Behandlung der Framboesia tropica mittels Bisuprol. [**Treatment of Yaws by Bisuprol.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Mar. Vol. 38. No. 3. pp. 118-124.

The author finds bisuprol to be an efficient preparation of bismuth in the treatment of yaws.

Yaws is widespread among the child population around Medan in Sumatra. In the earlier trials (1931) this drug in emulsified form was given in 2 cc. doses every three days for adults. The following year it was found that single doses of 10 cc. of a 6 per cent. emulsion (=600 mgm. colloidal bismuth), half each side intragluteally, were as efficacious and were an advantage in the case of a population whose attendance for treatment was irregular. The effect of this depot method of treatment probably lasts over 4 weeks. The results in secondary and tertiary cases were rapidly obtained while primary lesions were more resistant. With the larger doses pain was more marked but not sufficient to prevent their use. A few children developed stomatitis and one a fairly severe dermatitis; otherwise no unpleasant results were witnessed.

A certain number of patients were kept under observation by giving subsequent injections of saline, and it was in these that the excellent immediate results were noted. They were clinical results only. The ultimate results are unknown and no serological tests were carried out.

H. S. S.

GALINIER (Georges). La gangosa et les rhino-pharyngites mutilantes des tropiques. [**Gangosa and Rhinopharyngitis Mutilans of the Tropics.**—87 pp. [127 refs.] 1934. Paris: Jouve & Cie, Éditeurs, 15 Rue Racine.

A Paris thesis embodying observations made upon a single case of gangosa in Indo-China together with a study of some of the literature

on this condition. In a number of short chapters the history, definition, distribution, pathogeny, symptomatology, diagnosis, etc., are dealt with. Without bringing to light any new facts this brochure will form a handy volume of reference.

The author believes gangosa to be a disease *sui generis*, of unknown causation and differentiates between this condition and those similar conditions due to yaws, syphilis and leishmaniasis which he would include under the term rhino-pharyngitis mutilans. H. S. S.

TANI (T.) & OGIUTI (K.). Weiteres ueber die Meerschweinchen-frambösie. [**Yaws in Guineapigs.**].—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5. Vol. 131. No. 3/4. pp. 146-148.

A method of differentiating between the spirochaetes of yaws and syphilis by animal inoculation.

KAKISHITA showed that when an inoculum containing the "Manilla" strain spirochaete of yaws was injected into the testicle of the guineapig a metastasis appeared on the prepuce, and that infection into the preputium itself resulted in the production of a characteristic lesion which persisted for as long as 230 days. The authors have now repeated these experiments using a strain of yaws spirochaete from a Malay woman after three passages through rabbits. The spirochaete of yaws shows an affinity for the prepuce in contradistinction to the spirochaete of syphilis. H. S. S.

TURNER (Thomas B.) & CHESNEY (Alan M.). **Experimental Yaws. II. Comparison of the Infection with Experimental Syphilis.**—*Bull. Johns Hopkins Hosp.* 1934. Mar. Vol. 54. No. 3. pp. 174-185.

In this second communication [see this *Bulletin*, Vol. 29, p. 723] the authors report the results to date of their experimental yaws infections in rabbits comparing them with experimental syphilis infections in the same animals, the strains of *S. pertenuis* and *S. pallida* all having been obtained from Haiti as the purpose of the investigation was to obtain and experiment with strains of spirochaetes from cases of yaws and from cases of syphilis encountered in the same locality.

The surviving strain of *S. pertenuis* is designated "Y 9" and has been passed through 15 generations of rabbits. The strain of *S. pallida* is designated "strain K" and has been passed through 20 generations of rabbits.

In comparing the two infections in rabbits attention was focussed on (1) incubation period, (2) initial lesion after (a) intratesticular and (b) intracutaneous inoculation, (3) metastatic lesions, (4) seasonal variation.

Results went to show that no differences were noted in the experimental infection in rabbits inoculated with eight different strains of yaws virus. The disease picture produced by the yaws virus presented striking and for the most part constant differences from that produced by the Haiti strain of syphilis. The Haiti strain of syphilis gave rise to an experimental disease in rabbits which was similar in every way to that produced by several strains of syphilis virus isolated in the temperate zone. These results lend support to the view that yaws and syphilis are different diseases. H. S. S.

FIVOLI (Filippo). La sifilide indigena in Tripolitania (aspetti e profilassi). [**Indigenous Syphilis in Tripolitania.**—*Giorn. Ital. di Malat. Esot. e Trop.* 1934. June 30. Vol. 7. No 6. pp. 148-50, 153-6, 159-62, 165. With 6 figs.

A general account of syphilis as it occurs among the inhabitants of Tripolitania, the means adopted for its control and the results obtained.

In the Italian colonies of N. Africa syphilis is one of the principal causes of morbidity. It is more widely diffused towards the south and the interior than in the coastal regions and among the Arabs and coloured peoples than among the Jewish population, and the graver forms of the disease are associated with the higher incidence largely due to lack of resistance.

The disease as met with by Fivoli resembles that already described by others in similar populations. Among town dwellers it is contracted sexually but it is otherwise in the nomad peoples among whom ordinary hygienic measures and cleanliness are lacking, dermal parasitism is general and over-crowding the rule. Two special factors have also to be noted—prostitution and homosexual practices both among men and women. Patients seldom present themselves with primary lesions; the primary sore when seen (and in the male only) does not differ from that seen in Europe. That marked primary lesions with secondary infections would be seen under the conditions of filth which exist might be expected, but their absence is explained by the practice of circumcision.

Well marked differentiation into secondary and tertiary periods in the evolution of the disease is seldom witnessed. Earlier roseolar and papular eruptions may go unnoticed so that papulo-squamous lesions are most commonly seen often undergoing pustular and ulcerative changes; ecthyma and impetiginous lesions are common, and vitiligo is not uncommonly observed and of course not easily missed in darker skinned people. Associated lesions of the mucous membrane of the mouth and of the skin about the anus are general, the exciting factor for the former being, it is suggested, the use of hot condiments and excessive smoking. Gland enlargement is general but of no diagnostic value. Tertiary lesions often appear to overlap secondary lesions and frequently cannot be distinguished; secondary lesions often appear to be transformed into tertiary lesions after they have existed some time.

The greatest havoc is wrought upon bones, joints and muscles and with equal frequency the eye may be attacked—iridocyclitis. Very rarely are the viscera affected and still more rarely the nervous system.

The greater part of the cases coming under observation have already reached the tertiary stage and present ulcerative nodular and sclero-gummatous lesions of the skin, often very extensive and sometimes phagaedenic, together with gummatous lesions of palate and nose.

Abortion, premature birth and high infant mortality are considered to be due to syphilis. The commonest lesions in the congenital disease are snuffles, rhagades, keratitis, choroiditis, hydrocephalus, many dystrophies, infantilism, rickets, hare-lip, cleft palate and above all polydactylism, so common among these peoples [!]. Many lesions of the inherited disease cannot be distinguished from those of the acquired disease. [Such a statement as it stands should I think be received with reserve; many cases which might be considered as cases of inherited syphilis may in reality be cases of infantile infections. It is a question

constantly turning up in the consideration of native syphilis and remains unsettled.

In regard to the dystrophies mentioned above we see here reflected the ideas of the continental school. The reviewer would point out that many years ago writing upon congenital abnormalities in African natives (*Biometrika* 1914) it was shown how common they were, especially polydactylism, and this in a people among whom there was comparatively little syphilis.]

The anti-venereal measures adopted consisted in the regulation of prostitution and the provision of methods of inspection and treatment centres. This side of the question need not be further commented upon here.

H. S. S

BOENJAMIN (R.). Een proef met solganal B bij salvarsan-resistente framboesia tropica.—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Jan. 16. Vol. 74. No. 2. pp. 116-120.

MISCELLANEOUS.

LAMBERT (S. M.) **The Depopulation of Pacific Races.**—*Bernice P. Bishop Museum Special Publication 23.* 42 pp. With 11 figs. 1934. Honolulu, Hawaii. Published by the Museum. [Summary appears also in *Bulletin of Hygiene.*]

The paper discusses the effect of Europeans on native populations in Melanesia and Polynesia, and gives an account of the present state of these peoples.

The problem which Dr. Lambert has set himself to consider is fascinating in its complexity. The investigator must bear continually in mind that there are great differences in race, customs and outlook in different parts of Oceania. Furthermore, malaria is prevalent to the west of 170°E. but absent from Fiji and Polynesia, which lie to the east of that limit. Apart from this, the effects of European penetration have been extremely diverse, some of them greatly to our credit, others disgraceful. The trader, the missionary and the official had little enough in common, but they were equally effective in destroying much of the endemic social life; but their effect varied with different archipelagos according to the European Power which possessed itself of the islands and the missionary society within whose zone of activity they chanced to fall. As the forces at work have been numerous and conflicting, it is not surprising that their effect has been dissimilar. Some islands, for instance the Samoan group, were never gravely depopulated: from others the people vanished fifty years ago, and in others again they are now disappearing. The field worker, especially in Melanesia, will frequently observe great differences even between islands which are close to one another and in which the people, climate and diseases appear to be similar.

Dr. Lambert's work gives a good general account of the problem, and shows that the state of most of the populations is more prosperous than many Europeans believe. Without going exhaustively into the matter, he introduces the reader to some early travellers and their estimate of populations; then passing to modern times, he sets out such statistics as may be available. In this way he reviews most of the island groups of Melanesia and Polynesia.

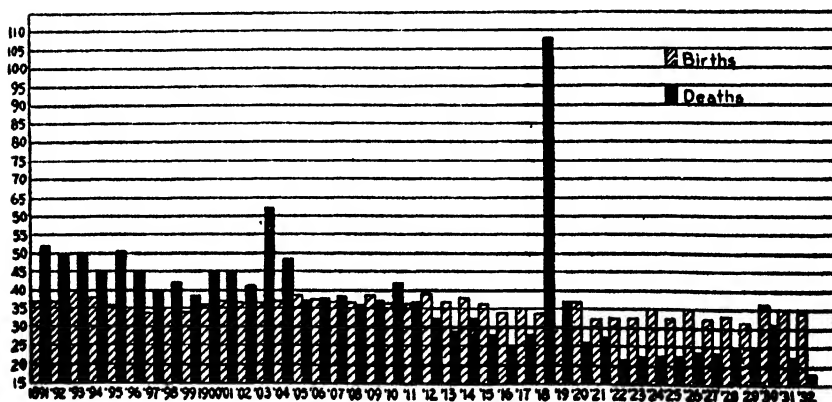


Fig. 1.—Native Fijian birth and death rates.

[Reproduced from *Bernice P. Bishop Museum Special Publication 23.*]

His treatment of Fiji may be considered here. It seems that births and deaths have been recorded in a trustworthy manner since 1891. The population at that time was 105,800 and it was declining (it was estimated at 300,000 in 1870). About 1905 the population, which had fallen to 87,000, became stationary, but since 1911 there has been a steady rise interrupted by the influenza in 1918. During the whole period since 1891 the births have been nearly stationary at about 35 per 1,000, but the deaths have fallen from 50 to 18 (fig. 1). The author's view is that this is due almost entirely to effective public health measures, and he mentions particularly campaigns against yaws, dysentery and hookworm. He rightly gives prominence to the work of the Native Medical Practitioners and to the importance of the Central Medical School at Suva, Fiji, which gives a solid practical course to suitable young men not only from Fiji but from other archipelagos. Within recent years infant welfare centres have been established in several parts of Fiji, and some at least of the reduction in mortality in the first five years of life is credited to them (fig. 2). The problem of Fiji is particularly complex, for the native race must not only adjust itself to Europeans but also to Indians, of whom large numbers have come in as indentured labour since 1881; but it seems clear that the adjustment has been made, and that the Fijian race is surviving.

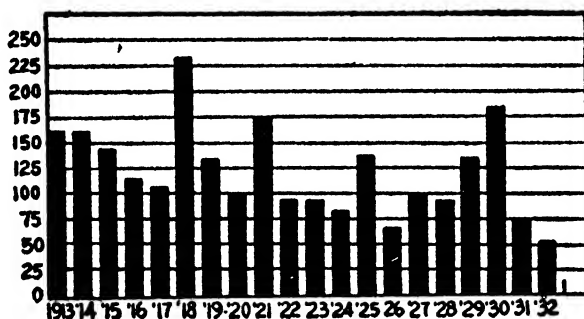


Fig. 2.—Fiji mortality of children 1 to 5 years of age.

[Reproduced from *Bernice P. Bishop Museum Special Publication 23*.]

Dr. Lambert's view may be summarized thus. There is no doubt that the depopulation was in some way caused by the white man. As to the causes we have little precise knowledge, but it is clear that introduced diseases were an important element. At the present moment the populations of most islands are stationary or rising. This may be due to a general adaptation to new life and introduced diseases, but it has clearly followed the introduction of preventive medicine, the direct effects of which are observable in a number of instances [the careful reader may discover for himself that the races which are still dying out are all administered under one flag, and that they receive less medical and sanitary help than the rest of Oceania].

As to the future and the grave menace of over-population of small islands, not a word is said.

P. A. Buxton.

LHÉRISSON (Camille). La patología de los campesinos haitianos. [Disease among the Rural Population of Haiti.]—*Bol. Oficina Sanitaria Panamericana*. 1934. Sept. Vol. 13. No. 9. pp. 821-834. With 8 figs. [22 refs.] English summary.

Plague, typhus and relapsing fever appear to be unknown, but almost every other disease of the tropics is found in Haiti. Enteric fever is common; dysentery also, both the bacillary and amoebic varieties. The former (Flexner and Shiga) is epidemic and, each year, is said to attack about 25 per cent. of the people; the latter is more common in the northern districts, affecting from 10-20 per cent. of the inhabitants. *Balantidium coli* is also met with. Geophagy is frequent among the children. In 1925 among 4,439 persons examined in 3 districts, 30 per cent. had hookworm, 43 per cent. *Ascaris*, and 58 *Trichuris*. Goitre is common in the mountainous regions and pinta in the plains. Tuberculosis is very fatal and in the hospitals accounts for 30 per cent. of the deaths. Malaria is rife; of 4,439 examined by the Rockefeller Mission staff 67 per cent. had parasites in their blood and of 11,000 emigrating to Cuba to work in the fields of the United Fruit Company 23.5 per cent. were infected. Subtertian predominates and the vectors are *A. albimanus* and *A. grabhamii*. The commonest of all diseases, however, is yaws; of 2,564 examined in the environs of Port-au-Prince 78 per cent. were suffering and among 3,289 cases, 61.9 per cent. were children under 10 years. The article contains an illustration of the crippling effects of this disease.

A National Public Health Service was established in 1919 and "the peasant is becoming every day more conscious of the value of health," but much remains to be done.
H. H. S.

PASCAL (J. M.). Essai médical sur le Mzab (Sahara algérois). [Mzab (Algerian Sahara) from the Medical Side.]—*Arch. Inst. Pasteur d'Algérie*. 1934. Mar. Vol. 12. No. 1. pp. 83-167. With 33 figs. (23 on 15 plates). [Refs. in footnotes.]

A complete account of this region of the Sahara from the medical side—its soil, climate, hydrography, inhabitants, native medicine and diseases. This annotation concerns chiefly the last.

The Mzab, lying on the northern edge of the Sahara, is a rectangle comprised between the 2nd and 5th degrees of east longitude and 31.3° and 33° north latitude. Ghardaia, its capital, is 480 kilos, as the crow flies, to the south of Algiers. Here the author practised for seven years. The climate is saharan. There is a difference of 17 degrees between day and night and 50 degrees between summer and winter. Air humidity is very low. In the last ten years the average rainfall has been 62 mm. The inhabitants consist of 22,000 Mzabites, 16,000 Arabs and 1,500 Jews; the first are of Berber origin and are the traders of the district. The diseases met with are discussed in order of decreasing importance—

Conjunctivitis. These patients make up one-third of those seen at hospital and more than half in spring and autumn. A table shows that in 37 bacteriological examinations the diplobacillus of Morax was met with 17 times, the gonococcus 3 times and the bacillus of Weeks twice. Trachoma is almost universal. There are eye dispensaries in every

village of more than 500 inhabitants and they are visited by a doctor at least twice a month. Most of the work is done by infirmiers but they are insufficiently paid and patients attend very irregularly. Excellent work in preventing the sequelae of trachoma is done at the schools.

Syphilis. Of 226 men who came to hospital (some for the treatment of their syphilis), 68 had clinical signs of the disease and of 134 who appeared to be free and whose serum was examined (Wassermann and Meinicke) 14 were infected, a percentage in all of 37. Primary lesions were rarely seen but penial scars were less uncommon. Three cases of tabes were seen in Mzabites in the course of 3 years. Rickets characterized by late appearance of incisors, late acquisition of walking and late closure of fontanelle is believed to be of syphilitic origin. It occurs in the Mzabites, Arabs and Jews in similar proportions to that of syphilis in those races.

Tuberculosis is manifested at consultation chiefly in the bones and glands. The author studied 2,334 persons by the cuti reaction (Parrot & Foley). For children between 1 and 15 years it varied between 42·5 in negroes and 49·7 in Arabs; for all ages it was 56·2, one of the highest indexes in the Sahara. The installation of a sanatorium is for reasons stated not practicable.

Typhus does not exist normally in the Mzab. It is suggested that inspection of arrivals from places where it has broken out should suffice for prophylaxis. Lousing centres are of limited utility because the natives do not care to entrust their families to foreign hands.

Enteric fever occurs sporadically and does not seem very harmful to the natives.

Diphtheria occurs sporadically, *scarlet fever* only when introduced.

Dysentery, rabies, plague, cholera, are unknown.

Tinea. One hundred scholars of each race were examined; there were found 20 trichophytic infections and 37 favus; only one case of favus was in Jewish children.

Helminthiasis. 80 per cent. of scholars harbour intestinal worms, the Jews less than the others. A full table records the data for each race. *Ascaris* is by far the most frequent, then come *Trichocephalus*, *Oxyuris* and lastly *Hymenolepis*. Of this last he remarks that there are no rats in the Mzab and that *Hymenolepis* eggs have not been found in mouse droppings. The gardens are manured with human dejecta which also soil the water supply.

Scorpion stings are common. Every summer one or two children under 8 die from this cause. The author has ceased to employ local treatment, having seen some deep burns caused by permanganate.

Of *bugs* he writes—The bug is an imported article . . . after its introduction the whole family seems to be suddenly attacked by a contagious disease with a rash—.

The only mosquitoes found by the author are *Culex pipiens* and *Theobaldia longiareolata*. Others have recorded *A. aegypti* at Ghardaia. Anopheles have never been recorded.

Leishmaniasis. Three cases of Oriental sore were seen in the spring of 1932 in children who had never left the Mzab.

Malaria occurs but always introduced from without. A. G. B.

KIRK (J. Balfour). **The Health Unit System as a Means of applying the Principles of Preventive Medicine in Rural Areas in the Tropics.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. May 9. Vol. 27. No. 6. pp. 587–592. [Summary appears also in *Bulletin of Hygiene.*]

Dr. Balfour Kirk, in his introductory remarks, lays stress on the fact which is common knowledge, it is true, but one of great significance in the Colonies, that the medical branch of the services, dealing mainly with curative treatment, has come to be regarded as distinct from the sanitation branch, dealing with hygiene and prevention, and further that the latter, being largely administrative and intimately connected with rules and regulations, and with penalties for infringement, "has become associated with compulsion," and all the world over compulsion implies resistance.

The author, who can speak with authority as one who has had considerable tropical experience, then states his conception of a rural Health Unit which has justified itself in Mauritius at least. This unit comprises a Dispenser, a Sanitary Inspector, a Health Visitor and a Midwife, and at the head a physician known as a Health Officer, who also is given the statutory powers of the Health Authority of his area. The duties of each are detailed and it is seen that, though there is the necessary cleavage between preventive and curative medicine proper, this is not so conspicuous because it occurs in the lower grades, in the subordinate staff. On epidemiological grounds (for example the early knowledge of something wrong or the beginning of an outbreak) this method is ideal in enabling prompt action to be taken.

Such a scheme would be particularly suitable in many, one might say most, of the tropical Colonies where the District Medical Officer is in charge of the local hospital and also acts as Medical Officer of Health of his district. This system moreover has the advantage of being capable of almost indefinite expansion without losing its essential characteristics. To those who have practised in the tropics the resistance—passive often, active sometimes—to any innovation is a matter of daily experience.

In an abstract one can do little more than point out the general trend of this valuable paper which should be read in its entirety and studied by all those practising in rural areas in the tropics. *H. H. S.*

MCKINLEY (Earl B.). **The Development of Tropical Medicine in the United States.**—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 299–307.

"Science" writes Dr. Earl McKinley, "has already learned more and has placed in the record more proven knowledge than the social and economic status of most tropical countries will permit of application." At the root of this failure to apply knowledge is poverty, for the methods of preventing disease must be of such low cost that the people can pay for them. He would have application of knowledge and search for new knowledge going on together, for only through continued research is progress made. He gives some account of the preliminary survey of tropical diseases which a committee of the U.S. National Research Council is carrying on. An attempt is being made to define the problem of disease in the tropical belt, *i.e.*, where certain diseases are prevalent, to what extent and with what distribution, and

enquiry is afoot as to what facilities are available for teaching and research. It is believed that when the problem has been defined both basic industries and private philanthropists will finance a public health program in the tropics. A. G. B.

WERNER (H.). Zur Frage der Akklimatisation der weissen Rasse im tropischen Tieflande. [**The Question of Acclimatization of White Races in Tropical Lowlands.**]—*Deut. Med. Woch.* 1934. Mar. 30. Vol. 60. No. 13. pp. 478-481.

An article devoted chiefly to the German colonization of Espirito Santo, Brasil and to North Queensland.

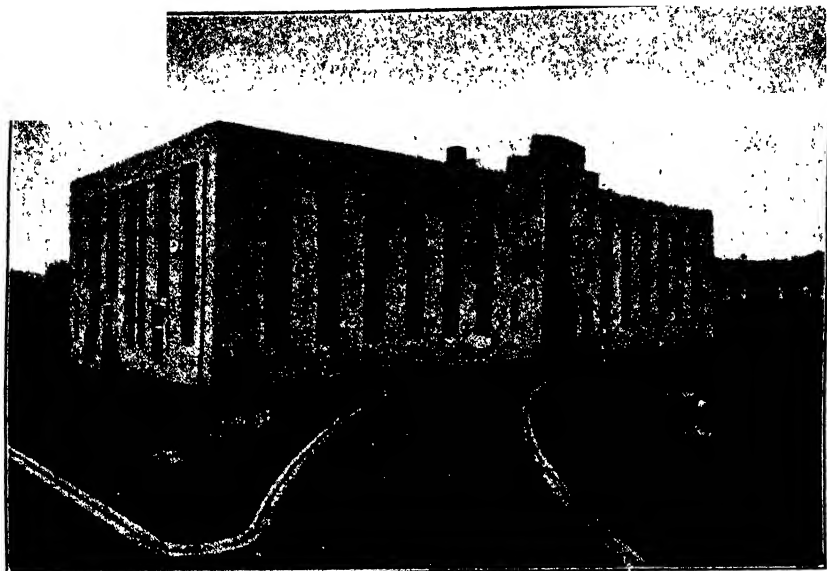
In the year 1847, 38 Rhenish families settled in Espirito Santo followed in 1857 [not 1897] by 280 families, in all about 1,000 persons. The birth-rate is given by WAGEMANN as 50-60 and the death-rate as 8-10 and the pure German population now numbers 17,000. The district settled lies between 17 and 22°S. on the eastern slopes of a mountain range. The average temperature is 20-21°C. Other data of temperature and precipitation are wanting but figures are given for the neighbouring town of Caripos on the coast. The region is described as marginal tropics (Randtropen) and it is questionable how far it should be separated hygienically as it is by the geographers from the real tropics (Innentropen). It is noted that settlement began on the highest ground and gradually worked towards the plains [see this *Bulletin*, Vol. 15, p. 296-7].

After consideration at some length of N. Queensland experience the author expresses the opinion that given the absence of certain diseases, such as malaria, yellow fever and hookworm, provided that indigenous races are kept at a distance or kept free from infection and that muscular work is performed by the white settlers, acclimatization of white races in tropical lowlands is possible and attainable. A. G. B.

HENRY LESTER INSTITUTE OF MEDICAL RESEARCH.—56 pp. With 41 figs. & 7 plans. 1934. Shanghai.

This attractive brochure gives an account of the inception and organization of the Henry Lester Institute, Shanghai.

Henry Lester, who died in May 1926, had by will directed that there should be founded "such building or buildings as may be advisable for the establishment of an institute or institutes for the study of medical science, surgery, civil engineering, architecture and other useful and scientific knowledge." It was decided that there should be two separate institutes, one medical, the other technical, and that the medical institute should take the form of a post graduate organization with emphasis on research. The scheme for the establishment of the Henry Lester Institute for Medical Research was approved in May 1928 and in the following year heads of departments were appointed to work in temporary quarters. In 1932 it was agreed that the Institute should consist of three main divisions—Clinical Research; Physiological Sciences; and Pathological Sciences, and at the end of the year the new building was entered. A Department of Medical Statistics was also formed, its first function being the collection of reliable statistics of the incidence of disease in different parts of China.



The Henry Lester Institute of Medical Research, Shanghai.

The building is here described. It is built on three floors with a basement and follows the unit plan, *i.e.*, all rooms can be regarded as consisting of one or more units, the dimensions of which are 12×18 feet; double units are 24×18 and so on, partitions being non-structural. Each floor is composed approximately of 40 units. The animal house is independent of the main building. The Director, Dr. H. G. EARLE, discusses the organization of medical research. Dr. James MAXWELL contributes a short article on the Library which has already 136 current periodicals. Other articles are by Dr. H. Gordon THOMPSON (Clinical Research and Experimental Surgery), Professor Bernard E. READ (Physiological Sciences) and Dr. R. Cecil ROBERTSON (Pathological Sciences). The illustrations consist of plans and of views of the various rooms. The Lester Chinese Hospital, which houses the Clinical Unit, is also illustrated.

No information is given of the funds at the disposal of the Institute; they must be assumed to be ample. A list is given of the scientific, and clerical and technical staff.

A. G. B.

SOUTH AFRICAN INSTITUTE FOR MEDICAL RESEARCH. Annual Report for the Year ended 31st December, 1933 [LISTER (Spencer), Director].—91 pp. With 2 plates & 1 chart. Johannesburg: P.O. Box 1038.

A large laboratory like the South African Institute for Medical Research naturally deals with a great many subjects and comparatively few of these are essentially of tropical interest.

The concentrated plague serum prepared in the Institute was tested on rats and showed that none of the virtue of the serum had been lost in the manufacture. Value and concentration were exactly parallel, which is a very important finding. Plague vaccine was investigated from the point of view of preparation of an endo-anatoxin which may

possibly prove more efficacious than the ordinary vaccine. It would certainly be an important advance to have an effective vaccine which gave little or no inoculation reaction.

The Flexner type of dysentery which occurs locally and seasonally is ordinarily of a mild and transient type. Flexner-like bacilli were examined in considerable number. Their particular characteristics were that they gave the biochemical reactions of the group but were inagglutinable with standard Flexner sera. It is still to be determined how far they are really pathogenic.

Some work has been done on the standardization of T.A.B. vaccine where recently isolated cultures were used, being first plated and the smooth colonies selected. The white mouse was the test animal used and it is capable of being protected by the vaccine against multiple lethal doses of virulent strains. A method of vaccination which is becoming increasingly popular is the use of typhoid vaccine tablets taken orally with bile pills. Evidently the efficacy of this oral method is to be made the subject of statistical investigation.

Anatoxins have formed subjects of study and of use in one form or another for some considerable number of years. At the South African Institute the same principle of reduction of toxicity has been applied to snake venoms. The products are "anavenoms" and they are used with great success in the rapid preparation of concentrated antivenenes of high potency. A research of a comparative type of Indian and South African venoms and antivenenes "with particular reference to their toxicities, the detoxication of Indian venoms and the cross action exerted by the respective concentrated antivenenes upon heterologous venoms," should prove very interesting. It is time, for example, that an authoritative answer was given to the question whether the antivenene prepared to the venom of one snake is of any avail against the venom of any other species of snake.

These are merely one or two of the subjects of interest in this annual report for 1933.

W. F. Harvey.

PEOPLE'S COMMISSARIAT FOR PUBLIC HEALTH S.S.R.A. [**Proceedings of the 3rd Congress on the Campaign against Malaria and Other Tropical Diseases in S.S.R. of Armenia held at Erivan 5-9 March 1931.**—164 pp. (State Publ. S.S.R.A., Med. Section) Erivan. 1933. [In Russian.] [4 roubles.]

This volume contains eighteen reports read at the above Congress. The majority (eleven) are on various aspects of malaria in the different districts of Armenia, such as incidence, economic importance, effect upon the population, prophylaxis, etc., and are of purely local interest. Amongst the remaining papers the following may be noted. According to MATEVOSSIAN (p. 82) during the last few years 20 cases of *Balantidium coli* infection have been recorded from Armenia, in some of which contact with pigs could be definitely established. TSATURIAN (p. 88) records 136 cases of acute and chronic amoebiasis during the period 1927-1930, the incidence being highest from the beginning of July to the end of September. EOLIAN (p. 113) draws attention to the wide distribution of echinococcosis in Armenia, which is associated with a high degree of infection in domestic animals (26 to 50 per cent. in dogs, 58 per cent. in cattle), and a low cultural level of the population living

in close contact with these animals. KARAPETIAN (p. 122) reports 18 cases of sprue between 1923, when the occurrence of this disease in Armenia was first recognized, and 1930. C. A. Hoare.

THOMSON (J. Gordon) & LAMBORN (W. A.). **Mechanical Transmission of Trypanosomiasis, Leishmaniasis, and Yaws through the Agency of Non-biting Haematophagous Flies.** (Preliminary Note on Experiments.)—*Brit. Med. J.* 1934. Sept. 15. pp. 506-509. [11 refs.]

The object of this preliminary note is to emphasize the important part which may be played by non-biting haematophagous flies in mechanical dissemination of blood-inhabiting organisms—a fact which appears hitherto to have been largely overlooked.

Most authorities are agreed that direct methods of infection by Tabanidae, Stomoxys, and other biting flies play an important part in the active spread of trypanosomiasis. Comparatively little work has been done on the transmission of the tissue-inhabiting pathogenic protozoa by Diptera other than biting species. CASTELLANI (1907) fed *M. domestica* on scrapings from yaws which contained *Treponema pertenue*, and afterwards, by transferring them to scarified sores on monkeys, produced an infection in one of the experimental monkeys. DARLING (1913) transmitted *T. evansi* to animals by means of house flies which infested the open sores on mules in Panama. LAVERAN (1880) suggested that oriental sore in Biskra might be due to transference of infection by flies, and WENYON (1926) stated that it was highly probable that the house fly which swarms round exposed oriental sores might sometimes carry the causative organism on its feet or proboscis to abrasions of the skin on another person; he likewise expressed the opinion that *Leishmania* bodies might pass rapidly through the gut of the fly and so be deposited with the dejecta.

In Nyasaland various species of muscids abound, and one in particular—*Musca spectanda*—has been shown by Lamborn to be almost entirely dependent on man throughout its whole life. The eggs are laid solely on human excreta, on which the larvae feed to maturity. The adult flies in the early morning settle on man, awaiting the opportunity to slake their thirst and deposit their eggs on his freshly excreted faeces. In one instance 35 female *M. spectanda* were captured in three-quarters of an hour from a linear scab half an inch long on the dorsum of the foot of a native.

It was these observations by Lamborn and the hypothesis put forward by him in 1932 concerning the part muscids may play in the spread, not only of trypanosomiasis, but also of cutaneous leishmaniasis, which led to the experimental work described in this paper. These experiments relate firstly to the mechanical transmission of *T. brucei* by *Musca spectanda*, secondly to the passage of living Leptomonads of the cultural forms of *Leishmania donovani*, *L. infantum*, and *L. tropica* through the intestines of *M. spectanda*; and thirdly to the passage of living *Treponema pertenue* through the gut of *M. spectanda*.

The authors summarize their results as follows:—

"1. Non-biting haematophagous muscids feed readily to repletion on blood, serum, serous exudate, ulcers, sores, and also secretions from the nose, eyes, and mouth. After a meal a certain proportion

of these flies pass blood or serum in their numerous dejecta, which may contain large numbers of living trypanosomes, leishmania, or the *Treponema pertenue* of yaws.

"2. These haematophagous flies have their preferred hosts—for example, *Musca spectanda* Wied, which occurs in great abundance in Nyasaland, favours man. It lays its eggs exclusively in human faeces, breeding very freely; it derives moisture from human faeces, and could thus take up *L. donovani* from this source, since the organism is known to occur sometimes in this medium. Large numbers attack persistently and with determination scratches, cuts, and sores of the skin of man in search of food, and also haunt the eyes, nose, and mouth in search of fluid.

"3. *Trypanosoma brucei* in the blood of rats and dogs are readily ingested by *M. spectanda*, and during a period varying between five minutes and six hours these flagellates can be passed alive in the numerous droplets of dejecta passed through the gut of the fly. Rats were experimentally infected by the intraperitoneal injection of these dejecta by placing a drop on a fresh cut on the ear and by placing the dejecta on a drop of blood exuding from the bite of a tabanid. *T. brucei* in the dejecta introduced into the eye, nose, and mouth did not produce infection. Certain flies after a feed extrude a drop of the ingested blood containing living trypanosomes from their proboscis five to ten minutes after a full meal.

"4. Living leptomonads in cultures of *L. donovani*, *L. infantum* (dog strain), and *L. tropica* are freely ingested by *M. spectanda*, and are passed viable in the droplets of excreta for several hours after a feed. There can be no doubt that these flies could ingest the round tissue forms of all the human forms of leishmaniasis and pass them in a viable state either through the gut or by regurgitation from the proboscis to sores or mucous membranes. It would seem certain that both kala-azar and oriental sore could be actively transmitted through the agency of these flies.

"5. *Treponema pertenue* of yaws passes rapidly in a viable form through the gut of *M. spectanda*, and so could easily be deposited on cuts and abrasions." W. Yorke.

CAZANOVE. Analyse de deux documents manuscrits du Docteur Peyre, Médecin-Chef de l'expédition de Saint-Domingue. [Two Manuscripts by Dr. Peyre, Chief Medical Officer of the San Domingo Expedition].—*Rev. Méd. et Hyg. Trop.* 1934. Mar.-Apr. Vol. 26. No. 2. pp. 65-91.

An account of the mortal illness and autopsy of General Leclerc, Captain General of San Domingo, who died of yellow fever there in 1802. His wife was Pauline Bonaparte. One gets a glimpse of the high fatality. Between February and November 1802 there died 1,500 officers, 750 doctors, 25,000 soldiers, 8,000 marines, 3,000 seamen, 2,000 employees and 3,000 whites from France. "Of this number only 5,000 perished by war, yellow fever harvested the rest." Besides other documents and discussions the paper contains a memorandum on the health service of the Navy and Colonies by Dr. PEYRE, Inspector General. A. G. B.

MANAI (Andrea). Contributo allo studio delle associazioni morbose. Nota IIa. Sui rapporti tra malaria e tubercolosi polmonare. [**Association of Diseases. Relations between Malaria and Pulmonary Tuberculosis.**—*Riv. di Malariologia*. 1934. Vol. 13. No. 4. pp. 443-473. [16 refs.] English summary.

The notion is fairly widespread that malaria and tuberculosis are mutually antagonistic; that where malaria is epidemic tuberculosis is uncommon; that malaria confers immunity against tuberculosis and that the malarious subject rarely contracts tuberculosis; that malaria can be employed in the treatment of tuberculosics in that it slows down the tuberculous process and leads to fibrosis.

The author has lived and worked for many years in Sardinia where both diseases are widely spread, and he has been able to observe many persons who have presented, sometimes contemporaneously, sometimes consecutively, the symptoms of both infections. His experience is at variance with the opinions expressed above. He finds that recent malaria seemed to act adversely on the course of an existent tuberculosis, and in patients with tuberculosis who seemed to be making satisfactory progress on subsequently contracting malaria the disease appeared distinctly to be aggravated, as if the malarial infection weakened or handicapped the body's defences. He infers, naturally, that malariotherapy is not suitable for phthisical patients. *H. H. S.*

BOGGIAN (Bruno). Esiste veramente un antagonismo tra malaria e tubercolosi? [**Are Malaria and Tuberculosis really Antagonistic?**] *Riv. di Patol. e Clin. d. Tubercul.* 1934. July 30. Vol. 8. No. 6. pp. 513-517. [14 refs.]

For many years, from about the middle of last century, there has been a vague belief that paludism and tuberculosis were mutually antagonistic. The author's experience is totally at variance with this. He quotes in detail four clinical cases and according to his experience he finds that malaria appears to give rise to an anergic state as shown by the subsequent reaction to tuberculin, von Pirquet's or Trambusti's method. This anergy, though it may be but transient, is definite. Again, he has repeatedly observed that a malarial attack has been followed by tuberculosis, sometimes pulmonary, at others of the serous membranes. Lastly, he has almost constantly seen that in a tuberculous patient the supervention of malaria has resulted in the lighting up and extension of the tuberculous process already existing.

H. H. S.

YENIKOMSHIAN (H. A.). Nonalcoholic Cirrhosis of the Liver in the Lebanon and Syria.—*Jl. Amer. Med. Assoc.* 1934. Sept. 1. Vol. 103. No. 9. pp. 660-661.

In the author's experience hepatic disorders are common in Syria and the Lebanon, due to disease of the biliary tract, to hydatid and to amoebiasis, but apart from these is a group exhibiting hepatic enlargement with splenomegaly. It is with these last that the present article deals.

Many of the patients suffer from repeated febrile attacks with jaundice, transient enlargement of the liver, epigastric tenderness, nausea and vomiting, the attacks lasting perhaps for a few days only, but sometimes for weeks. The author found it more among farmers

and the rural population than among city dwellers, and mostly among those dwelling in villages near Tyre and Sidon.

During a period of six years he has seen in the wards 70 cases of portal cirrhosis with ascites; about two-thirds of the patients were under 40 years of age, and 20 per cent. were under 20 years; males affected were rather more than twice as numerous as females. Splenomegaly in most cases appears long before the ascites, and palpation reveals a hard, irregular liver which is enlarged to the end, and a large spleen and hobnail liver are seen at autopsy. [In temperate climates hobnail liver with ascites is usually reduced in size.] The causation is obscure. The diet does not appear to be responsible. It is largely vegetarian and cereal; mutton is eaten, beef, chicken and fish only occasionally. The men rarely and women never drink alcohol. Malaria and dysentery are common, as also are helminthic infestations, in order of prevalence, *Trichuris trichiura*, *Taenia saginata*, *Ascaris lumbricoides* and *Enterobius vermicularis*. Ankylostomiasis and filariasis are rare and there is no schistosomiasis. Syphilis is uncommon.

The author is of the opinion from a prolonged study of these cases, both from the clinical and pathological aspects, that chronic malaria and amoebic dysentery, especially when combined, are important aetiological factors.

H. H. S.

GILLAN (Robert U.). **An Investigation into Certain Cases of Oedema occurring among Kikuyu Children and Adults.**—*East African Med. Jl.* 1934. June. Vol. 11. No. 3. pp. 88-98.

A condition is described in small children and in women having some of the characters of coeliac disease and sprue. A toxæmia of origin in the small intestine is suspected.

The author kept notes of 12 cases, seen in 2-3 years; 9 in children all breastfed and 3 in women. There was generalized oedema, pallor, patchy desquamation of the skin and depigmentation of the hair; the oedema was the chief feature and was sometimes so severe as to cause occlusion of the palpebral fissure; there was no albuminuria. The children were extremely irritable and resented exposure. A history of 7-9 months illness was usual. Diarrhoea was usually noted. Blood counts indicated anaemia of varying intensity. The stools were large, pale, greasy or soapy looking, greyish and sour to the smell. Five patients died in hospital and possibly others outside.

The diagnosis is considered in relation to coeliac disease, sprue, pink disease and beriberi. One stool was examined by a biochemist who reported a high percentage of saponified fat; this is believed to be due to the diarrhoea and not to deficiency of biliary or pancreatic secretion. Histological examination revealed a severe chronic enteritis. Indications for further investigation are given.

A. G. B.

MAEGRAITH (Brian); McCLOSKEY (A. J.). **Pineapple Juice in Oedema.** [Correspondence.]—*Brit. Med. Jl.* 1934. Sept. 8 & 22. pp. 492; 572.

Dr. Maegraith mentions the case of a patient, a woman of 30 years, suffering from oedema of cardiac origin who had been treated by digitalis, mercurials, etc., but without success. The oedema affected back and legs and there was also double pleural effusion. She was given the

juice from a tin of pineapple daily and in a fortnight the oedema of trunk and legs subsided, the urinary output increased from 18–20 oz. to 60–100 oz. in the 24 hours, and in another week the pleural effusion cleared up. After leaving hospital she continued to eat one tin of pineapple a week and when she reported herself some months later she was still free from oedema.

Dr. McClosky follows the above communication by stating that in the course of an outbreak of beriberi in the gaol of Kuala Lumpur in 1896–98, the "Chinese patients with dropsy invariably asked for pineapple." He gave it as a placebo and the dropsy subsided, but unfortunately for the test they were given other diuretics also. He mentions that Chinese patients with wet beriberi in other State Hospitals also used to ask for pineapples. The treatment is worth further study.

H. H. S.

MONCRIEFF (Alan) & WHITBY (L. E. H.). **Cooley's Anaemia.**—*Proc. Roy. Soc. Med.* 1934. Aug. Vol. 27. No. 10. p. 1324 (Sect. for Study of Disease in Children p. 56).

— & —. **Cooley's Anaemia.**—*Lancet.* 1934. Sept. 22. pp. 648–649. With 1 chart.

The case here described would formerly have been classed as von Jaksch's anaemia, but the conditions present several differences from the latter as understood by English paediatricians. Attention was first drawn to it by T. B. COOLEY, an American physician, in 1927. The patient is nearly always of Mediterranean stock; the subject of the present article was a girl of 1½ years old born in the Middlesex Hospital of Greek parents. The findings were typical: erythrocytes in the neighbourhood of 3 million per cmm., Hb. 38–40 per cent., leucocytosis about twice the normal. The biochemical investigations are detailed in the report to which those interested should refer. Radiographically, all the bones showed generalized rarefaction; the skull bones thinning of the tables and increase in medulla. Post mortem the skull bones were very soft, and the bony tissue of the femur very thin, with marrow a dense dark red. The spleen was a little enlarged as was also the liver. The condition has been named Cooley's anaemia from the physician who first described it; another name is "thalassaemia" on account of its predilection for the Mediterranean races.

H. H. S.

MCRÖBERT (George R.). **The Treatment of Bacterial Food Poisoning.**—*Brit. Med. Jl.* 1934. Aug. 18. pp. 304–305.

The author has abandoned the use of purgatives in bacterial food poisoning, so common in the tropics and now relies entirely on the absorptive action of kaolin, preferably a preparation of "colloidal" kaolin, which serves to detoxicate the bowel while soothing and protecting its lining. In a severe case treatment by rest in bed with warm bottles, gum-saline or Rogers' hypertonic saline is supplemented by the oral administration of 2 drachms to the wineglassfull of kaolin, after which morphine may be injected without harm. One drachm of kaolin is advised every 15 minutes until the diarrhoea is controlled. In less severe cases frequent kaolin and large quantities of water are advised. The author regards the introduction of fine kaolin as one of the most important recent advances in practical everyday therapeutics.

A. G. B.

PALMER (F. J.). **Hot Weather Ear—a Clinical Entity.**—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 430–432.

This is a condition seen in soldiers in Assam and elsewhere in India in which the ear becomes painful, the meatus is more or less blocked by swelling and a ring of skin eventually separates. The treatment is described. The author suggests it is a ringworm infection with probably a bacillary one added. Most cases occur in the hot weather.

A. G. B.

NOOSTEN (H. H.), KIRSCHNER (L.) & VOS (J. J. Th.). **Rhinoscleroma op Bali. [Rhinoscleroma on Bali Island.]**—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. July 3. Vol. 74. No. 14. pp. 835–852. With 1 fig., 1 map & 51 figs. on 4 plates.

A focus of rhinoscleroma had been described upon the island of Samosir in the Toba lake, Sumatra (this *Bulletin*, Vol. 30, p. 49) and the view promulgated that this was a disease of primitive people. Now a new focus has been found by the authors upon the island of Bali.

The disease, which is infectious, has its seat in the respiratory tract and may occur anywhere from the nares to the hilum of the lung. It is an infiltrative condition, slowly and continuously progressive, without necrosis or ulceration and is terribly disfiguring. A causal organism, one of the capsule bacilli, is found and can be distinguished from the pneumobacillus and the ozaena bacillus by serum tests. Histologically the scleromatous tissue is found to be permeated with plasma cells but most characteristic of the condition are the so-called cells of MIKULICZ, which are in all probability swollen and degenerated endothelial cells. As a culture medium for the bacillus, Drigalski agar is better than ordinary agar, for then the growth of cocci and of proteus bacilli is inhibited. Nine clinical cases are described as being typical, although there were others which were almost certainly also cases of rhinoscleroma. A differential diagnosis by histological, bacteriological and serological means could be made of the affection from nasal polypi, chronic inflammations of the nasal accessory sinuses and from pathological processes due to syphilis, yaws and leprosy. The authors do not think that these cases are restricted to northern Sumatra and Bali and they expect that reports of their occurrence will in due course be forthcoming from Java and other places. Therapeutic measures range over autovaccines, protein therapy, artificial malarial infection: and gold preparations but the most favoured method of treatment is by irradiation, although it may be followed by unpleasant complications.

W. F. Harvey.

CASTELLANI (Aldo). **Elephantiasis Nostras (Non-filarial Elephantiasis).**—*Proc. Roy. Soc. Med.* 1934. Mar. Vol. 27. No. 5. pp. 519–523 (Sect. of Trop. Dis. & Parasit. pp. 25–29).

The cases described were contracted in non-filarial countries—Great Britain, Italy, the Balkans and parts of the United States, and their elephantiasis is held to be of bacterial origin.

For detection of bacteria the lymphatic glands must be examined, and this must be done when lymphangitis and lymphadenitis are actually present. The organisms are of 4 groups, gram-positive staphylococci probably of little aetiological import, gram-positive streptococci

mostly of haemolytic type, gram-negative *Micrococcus mycelicus* which are more likely to produce slowly developing abscess or sinus than elephantiasis, and *M. metamyceticus* whose subcultures may vary in their staining reaction. The sequence of pathological change is—acute bacterial lymphangitis and lymphadenitis usually starting from some small lesion, perhaps an epidermophytic crack, oedema at first fluid and then solid, and hyperplasia of skin and subcutaneous tissue. During acute lymphadenitis, the enlarged and congested gland shows many thickened and perhaps thrombosed vessels, with the lymphoid tissue but little changed; later there is fibrosis with atrophy of this tissue. The main changes in the dermis are—lessened bulk of individual epithelial cells with loss of prickles and corresponding approximation of nuclei, and many dilated lymph spaces, thickened arterioles, and fibrosis; symptomatology and site are as for filarial elephantiasis and the condition is progressive. Diagnosis depends on place of residence and antigen-based tests. In the acute stages well-diluted salicylates are advised, 10 to 15 grains [0.6 to 1 gm.] thrice daily; in the chronic, weak vaccine doses 10 to 100 millions every 4th or 5th day; in the pachydermatous stage, a month in bed half-yearly with bandaging and fibrolysin injections. Any operation should be preceded by a vaccine course.

In discussion MANSON-BAHR classified the causation. MacCORMAC quoted HANDLEY's opinion that lymphatic obstruction will not alone cause elephantiasis, but that the resultant fibrosis will obstruct neighbouring veins. Parkes WEBER alluded to the congenital group. Hamilton FAIRLEY stressed the focal nodes of filarial elephantiasis and the intradermal test as distinguishing the two forms of the disease.

Clayton Lane.

MORALES-OTERO (P.) & POMALES-LEBRÓN (A.). **Antistreptolysin Content of Sera from Cases of Recurrent Tropical Lymphangitis.**—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1170-1172.

A contribution from the School of Tropical Medicine, University of Porto Rico. The antistreptolysin values of the sera of 41 patients suffering from recurrent tropical lymphangitis and of 20 normal subjects are reported. The antistreptolysin titre is increased in the former series: here 3-figure values are usual, in the normal subjects they are rare. The serum of two acute lymphangitis cases varied in antistreptolysin titre before, during and after the attack. A. G. B.

REVIEWS AND NOTICES.

KOLLE (W.) [Director, Inst. Experim. Therap. & Chemiotherapeutical Res. Inst., "Georg Speyer-Haus," etc.] & HETSCH (H.) [Professor Inst. Experim. Therap., Frankfurt]. **Experimental Bacteriology in its Applications to the Diagnosis, Epidemiology, and Immunology of Infectious Diseases. Vol. 1.** [Edited by John EYRE, F.R.S. Edin., F.Z.S., M.D., M.S., D.P.H., Director Bact. Dept., Guy's Hosp., etc.]-592 pp. With 118 plates & 200 text figs. 1934. London: George Allen & Unwin Ltd., 40 Museum Street, W.C.1. [30s.] [Review appears also in *Bulletin of Hygiene*.]

This is the first volume of the translation of the well-known and standard German text-book "Experimentelle Bakteriologie" by Kolle and Hetsch. The work has already reached a seventh German edition and has been translated into several languages. Originally based on lectures to University students it is refreshingly free from the faults of compression. Though it makes a somewhat large book it is easy to read continuously and with interest, a rather unusual feature in bacteriological text-books. It is based more than most modern text-books on tradition and it is most sound and interesting when on the older and well beaten tracks of bacteriology. Any teacher or student of bacteriology would profit by reading "Kolle and Hetsch" if only because it gives an excellent idea of the best German teaching, but it has an appeal to more specialized classes of readers. Both the student of clinical medicine and of public health may obtain an excellent general idea of what bacteriology has accomplished in those spheres, and what is still more valuable—an idea of how the bacteriological outlook may illuminate other branches of medicine. Over and above the general treatment there are several chapters of special excellence. The account of cholera, typhoid, anthrax and many other diseases could hardly be bettered as single chapter accounts, not merely as bacteriology but as general descriptions of those diseases.

To students of tropical medicine the book is particularly adapted, not only for the wealth of information it provides on infective (including protozoal) disease but also because it illustrates so admirably a point of view absolutely necessary to the tropical practitioner, that no line can be drawn between clinical and laboratory knowledge. The numerous illustrations, many of them in colour, which have been such an admirable feature of the German versions are beautifully reproduced. The translation of such a work is a formidable undertaking which on the whole has been carried out satisfactorily. The inevitable typhus for typhoid has been allowed to escape in one or two places. And in such chapters as that on gas-gangrene not enough trouble has been taken to link up English and German nomenclature. These are, however, but small faults in an otherwise admirable version. *C. C. Okell.*

KNOWLES (R.). **The Calcutta School of Tropical Medicine 1920-1933. An Essay-Review.**—*Supplement to Ann. Rep. of the School for 1933.* pp. 168-xlvii. 1934. Bengal Govt. Press.

Col. Knowles, who was concerned with the Calcutta School in its prenatal days, who officiated at its birth and has been intimately connected with it ever since, is eminently fitted to describe its early

development and the result is worthy of his facile pen. It starts with a brief review of the financial and administrative difficulties which surrounded its inception, and he gives full recognition to the energy and enthusiasm of Sir Leonard ROGERS, who is in fact the founder of the School, and also to the influence exercised by its successive directors, Sir John MEGAW and Lt.-Col. H. W. ACTON. It is a particular cause for congratulation that generous financial support came from some of the Calcutta business community, and the fact that their support is still being maintained in spite of economic depression augurs well for the continued co-ordination of science and industry founded on reciprocal benefits. Col. Knowles gives a short account of the work of the School as a centre for post-graduate training in tropical diseases and in public health. Though his reference is brief it is questionable whether this is not the most important of the School's activities in view of the fact that the safeguarding of India's public health will, in the near future, lie largely in the hands of the rising generation of Indians.

The third part of the review deals with work past, present and future of the major researches carried on at the School and to this part tropical workers will naturally turn.

Of their many successes we may make special mention of the *kala azar* problem, particularly the part played by the sandfly and the preparation and testing of the antimony compounds as well as of the careful epidemiological observations thereon. The use of the pentavalent antimony compounds represents one of the most dramatic and successful therapeutic discoveries of the century and in this triumph the Calcutta School can rightly claim a share.

Valuable work has been done in *malaria*, particularly that concerned with the disease in monkeys, which is another of Knowles' personal successes. The discovery of an animal susceptible to a disease is always the key-point in its elucidation and so it comes that the transmission of human malaria under controlled conditions and of monkey malaria has already thrown more light on the problems of malaria and blackwater fever than a generation of laboratory and field work had been able to accomplish.

The *dysenteries* have received a good deal of attention without there being much progress to record, whilst regarding *sprue*—well, anyone who still entertains any lingering doubt regarding the pathogeny of this mysterious disease should now have his doubts dispelled, so simple does it all appear!

Cholera research largely resolves itself into a consideration of the bacteriophage problem, the complexity and controversial nature of which is well known. The relation between agglutinable and non-agglutinable vibrios is still unsettled and according to these researches this is dependant on the permutations and combinations of ten specifically different bacteriophages. Despite this confusion "the manufacture of bacteriophage for Government hospitals is now an important part of the work." "Trying it on the dog" with a vengeance! The section on *hookworm* and *filariasis* is comprehensive, and LLOYD's observations on the complement-fixation reaction in the latter disease are interesting. He shows that some cases give a positive reaction together with eosinophilia whilst others show a negative reaction with a polymorphonuclear increase, suggesting that local sepsis conceals or destroys the antigenic reaction due to the presence of the worms. The work of MUIR on *leprosy* has brought much credit to the Calcutta School, but despite the volume of work performed here

and in other parts of the world we are still unable to determine the actual curability of this disease. It is good to learn that of a number of remedies, hailed with enthusiasm and abandoned with regret, some remain which give promise of more permanent value.

The Calcutta workers themselves have helped to tone down the extravagant optimism of twenty years ago and to show that the building up of the lepers' resistance and the treatment of intercurrent disease has as least as much value as the use of any particular drug. Space does not permit a detailed reference to other subjects of major research namely epidemic dropsy, lathyrism, diabetes, spirochaetoses, the indigenous drugs and the drug addiction enquiries, and diseases of the skin and respiratory system.

The fourth division of the Essay-Review is taken up by departmental reports and the work undertaken by each in chronological order. There is necessarily a good deal of repetition and overlapping in this part of the review, but it contains much interesting routine work and the record of minor researches which have been essayed but not brought to maturity.

MEGAW's description of tick typhus in India is an outstanding contribution to the Tropical Medicine Section and is one of the few major contributions to purely clinical medicine.

Col. Knowles ends his 168 pages with a brief note regarding the "future" and one is glad to find that his superabundant optimism still holds and is an answer to those who experience "that sinking feeling" when contemplating the full Indianization which approaches so rapidly. Col. Knowles with his gift (almost one might write "urge") for self expression has carried out the analyses of the School's activities (together with that of 740 original papers) in the true Boswellian spirit. He deserves well of his School whilst the rest of us will be grateful for his description of the work of this already distinguished institution.

F. P. Mackie.

HEGLER (C.) & NAUCK (E. G.). *Tropenkrankheiten. [Tropical Diseases.]*—Reprinted from MOHR & STAEHELIN's *Handbuch der inneren Medizin*. Dritte Auflage. Erster Band. Infektionskrankheiten. pp. 1098-1212. With 67 figs. (14 coloured).

Within the limits of about a hundred pages Drs. C. Hegler and E. G. Nauck, of Hamburg, describe the following diseases: malaria, blackwater fever, relapsing fever, rat-bite fever, sleeping sickness, kala azar, Chagas's disease, dengue, papataci fever, Japanese river-fever and yellow fever. Of these diseases the only ones that are dealt with at all fully are malaria, blackwater fever and yellow fever; but in the descriptions of the other subjects, though they are necessarily very compressed, very little of importance seems to have been omitted. The accounts given of the pathology and morbid anatomy of the various diseases are especially good, and the illustrations, many of which have been borrowed from other books, have been carefully selected and are very satisfactory. As there are already in existence several excellent German books on Tropical Medicine, it is presumably for the sake of completeness that this section forms part of the first volume of the large work on Medicine founded by Drs. Mohr and Staehelin: the authors show such a practical firsthand knowledge of their subject that one cannot help regretting the limitation of space imposed upon them.

H. J. Walton.

ROCKEFELLER FOUNDATION. **Annual Report 1933** [MASON (Max), President].—pp. xix+477. With 40 illustrations. New York: 49 West 49th Street. [Review appears also in *Bulletin of Hygiene*.]

In a foreword to this report, the president states that "the Foundation is dedicated to the welfare of mankind," and it is certainly in this spirit that its many activities are carried on. Wherever there is need of it, in both hemispheres of the world, substantial help is given to any undertaking which is working to promote improvement in Public Health or useful knowledge. During the year 1933 demonstrations of the practical application of various health measures were given in many countries; and funds were provided for the establishment of public health laboratories, for resident and travelling fellowships, for training in midwifery, nursing, sanitary engineering and other cognate subjects. In China and in Java the Foundation representative is adviser to the Government; in the former country he is also professor of hygiene, and Head of the department of public health at the Peiping Union Medical College. As the report says: "the Foundation is not committed to any one country or place. It can follow a problem wherever that problem develops, and thus gain experience in handling situations under a great variety of conditions."

Those parts of the report which deal with public health and medical science describe much research work both in the laboratory and the field.

An extensive survey was made in 1933 of the areas in Africa in which yellow fever occurs. This was facilitated by the discovery that *Macacus rhesus* and white mice are susceptible to the disease, and by the application of the "protection test" (i.e., the ability of the blood-serum of a person who has recovered from yellow fever to protect mice from infection). It was found that yellow fever in a mild form may exist for years as an undetected disease. In French Equatorial Africa, where yellow fever had never been reported, over eighteen per cent. of the blood specimens collected in thirty-seven towns, both on the coast and in the interior, protected white mice against the virus. As in former years, the Foundation has worked at the control of yellow fever in Brazil. In that country a system of routine microscopic examination of liver-tissue, from persons who had died after brief febrile illnesses, was found to be very effective in the detection of unsuspected cases of yellow fever.

Much antimalarial work was done in many places. Extensive mosquito surveys were made in the Amazon valley, the Philippines, Greece, Panama and elsewhere. A certain strain of a plasmodium from the canary (*P. cathemerium*), obtained from Rome, was maintained for ten months by bi-weekly passages, during which time it failed to produce any gametocytes, though another strain from the same source continued to produce the sexual forms of the parasite.

From the study of dogs, infested with *Ancylostoma caninum*, it appears that the anaemia is not caused by any special toxin; it results from direct haemorrhage, and responds well to treatment with iron. Seven cases of acute hookworm disease were observed at Porto Rico; the disease seems to have been contracted by bathing in highly polluted seawater. The symptoms came on suddenly, with dermatitis followed by much discomfort in the throat; within two to four weeks, colic and diarrhoea appeared. The patients were unusually weak, pale, and lost weight rather rapidly. A description is given of a larval variety of

hookworm disease, characterized by loss of strength and weight, anaemia, irregular fever, high eosinophilia and leucocytosis. There are few, or even no worms at all, in the intestine, and, in the latter case, absence of ova in the stools; the diagnosis may be difficult. It is thought that, in such cases, only a few larvae have been able to reach the intestine, the others remaining in the tissues of the body.

Research and routine work were done in many other tropical diseases besides those already mentioned.

The annual Report of the Rockefeller Foundation is always interesting, and the interest is fully maintained in that for the year 1933. The work is evidently carried on with great enthusiasm, and it owes much of its success to the admirable organization at the Centre.

H. J. Walton.

PITTALUGA (Gustavo). El tratamiento del paludismo. [**The Treatment of Malaria.**—96 pp. [9 pages of refs.] Coleccion de Monografias de "Los Tratamientos Actuales." 1934. Madrid. [250 pesetas.]

This is the first of a projected series of monographs on modern treatment, and if the others are as good as this the series will be a valuable one. In a handy little volume of 100 pages the most recent views on the treatment of malaria are presented. Professor Pittaluga deals with the subject under the following headings: (1) The acute primary attack, subtertian, benign tertian and quartan; (2) Recrudescence and relapse; (3) Chronic and latent infections; (4) Anomalous forms, mixed infections, haemoglobinuric fever, quinine idiosyncrasy, etc. He devotes a chapter to experimental malaria and a pharmacobiological study of new drugs. Having considered each of these in detail, the author devotes a final chapter to a summary and recapitulation. The work concludes with a good selective bibliography of nearly 100 references of which more than one-third are British.

H. H. S.

WENCKEBACH (K. F.). Das Beriberi-Herz. Morphologie. Klinik. Pathogenese. [**The Beriberi Heart.**—(Pathologie und Klinik in Einzeldarstellungen, Bd. vi.) pp. vi+106. With 38 figs. 1934. Berlin & Vienna. Verlag von Julius Springer. [Rm.12; Bound 13-50.]

The observations recorded in this monograph were made by Professor Wenckebach a few years ago in the Dutch East Indies and Singapore. He was able to conduct post-mortem examinations on a number of cases of beriberi, and taking the precaution of injecting a hardening fluid shortly after death he confirmed the presence of certain gross anatomical changes as characteristic of the disease. These changes were for the most part demonstrable during life by means of radiography. The whole of the right side of the heart, including the conus arteriosus, was always greatly enlarged while the left side remained comparatively small. The large systemic veins were enormously distended; as much as 3 litres of blood sometimes escaped from incisions made in the region of the right auricle. The extra-pericardial pulmonary vessels on the other hand were not abnormally congested. Microscopic examination of the heart muscle after death revealed changes of the nature of intracellular oedema, sarcolysis, hydropic degeneration and so on. These changes were by no means constant,

hence it did not seem likely that primary changes in the efficiency of the heart muscle could explain the entire clinical picture of heart failure in beriberi.

The clinical signs in well developed cases were cardiac enlargement, murmurs, often inconstant and transitory, a rapid bounding pulse, enlarged liver and congested veins, a normal or raised systolic blood pressure with a low diastolic pressure and swelling of the calves without visible oedema. The clinical picture suggested that abnormalities in the peripheral circulation might be responsible in part for the heart failure. This suggestion received support from the observed results of injections of adrenalin and pituitrin. In convalescent cases adrenalin produced a striking return of the signs and symptoms, causing an increase in the venous pressure and pulse rate and a lowering of the diastolic blood pressure. These effects were interpreted as being due to a dilatation of peripheral arterioles leading to a sudden flooding of the right side of the heart. Pituitrin, on the other hand, had exactly the contrary effect, causing a fall in venous pressure and pulse rate and a raising of the diastolic blood pressure; at the same time the subjective symptoms were greatly improved. These effects were ascribed to an increase in the tone of peripheral arterioles.

In his summing up the author puts forward the hypothesis that the primary cardiac lesion in beriberi is a loss of contractility of the heart muscle, possibly related to increased water retention within individual muscle fibres. Associated with this cardiac lesion is a loss of peripheral vascular tone which intensifies the signs and symptoms of cardiac insufficiency. The possible rôle of ductless gland disturbances in bringing about the cardio-vascular changes is considered worthy of further investigation.

S. J. Cowell.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 2.]

KALA AZAR.

BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1934. Aug. Vol. 26. No. 8. pp. 1369-1395.—La leishmaniose viscérale dans les pays méditerranéens [pp. 1369-1370]. Le kala-azar en Yougoslavie [TARTAGLIA (P.) pp. 1371-1381. With 2 maps.] Sur la répartition géographique des leishmanioses en Algérie d'après les documents de l'Institut Pasteur d'Alger [pp. 1382-1385. With 1 folding map.] Les leishmanioses en Égypte [KHALIL (M.) pp. 1386-1392. With 1 map. [22 refs.]]. La leishmaniose viscérale en U.R.S.S. [pp. 1393-1394]. Les leishmanioses en Perse [COULOGNER, p. 1395]. [*Leishmaniasis in Mediterranean Countries.*]

At the First International Congress of Hygiene for the Mediterranean (1932) it was decided that information should be sought regarding the distribution of kala azar in the Mediterranean basin. Accordingly the International Health Office in Paris and the Health Committee of the League of Nations joined forces and sent a questionnaire to the various countries concerned. Replies have been received from several countries but except for the information regarding kala azar in Yugoslavia and oriental sore in Egypt little that is new is forthcoming.

As regards Yugoslavia the author says that 89 cases of kala azar have been diagnosed, two-thirds by the discovery of parasites. The cases are limited to the southern half of the Adriatic coast but it is pointed out that this distribution is merely the result of the limitation of the inquiry to this part of the country. Undoubtedly with further experience and investigation the area will be extended. The disease has evidently existed for a long time, in spite of the fact that the first case was not diagnosed till 1930. In character it resembles that of other endemic centres in the Mediterranean and occurs chiefly in children, though adults are not exempt, as shown by seven cases, one of which was in a military surgeon 47 years of age. Canine kala azar has also been discovered, but no special association with the human disease has been noted. Sandflies are prevalent.

With reference to Algeria no new information is given and the same remark applies to Persia, the U.S.S.R. and Egypt as far as kala azar is concerned. Under Egypt, however, some recently acquired knowledge of oriental sore in this country is given. An endemic centre consisting of five heavily infected villages has been discovered to the north

of Zagazig. In the five villages 1,384 of the 1,408 inhabitants were examined, with the result that 232 showed active sores and 341 scars of healed sores. Investigations to the south and east indicate that the endemic area is about 30 kilometres in diameter, the number of cases diminishing as the distance from the village Kafr Ageeba increases. It is probable, however, that the endemic area will be found to extend to districts further north and west when these are examined. Cases of oriental sore in Egypt have occurred singly from time to time since its first detection by FERGUSON and RICHARDS in 1920, so that the discovery of this heavily infected centre is very striking.

C. M. Wenyon.

CAMINOPETROS (J.). Nouvelles données épidémiologiques et expérimentales sur les leishmanioses en Grèce. [**Leishmaniasis in Greece. Epidemiological and Experimental.**]—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 443-450. With 3 figs.

The author discusses the distribution of human and canine kala azar in Greece and is able to point out that of 46 human cases seen during the course of 1933 and the beginning of 1934 in Athens 18 were from Athens itself, the others having come from various parts of the country, showing that the disease is widespread.

As regards the canine disease the author has seen 31 cases from Athens or the villages of Attica. Cases of the human and canine diseases have also been discovered in the Peloponesus, Kalamata and in the islands of Soetzia and Syra. At the end of the paper the author states that he has produced a generalized infection in a spermophile by the intrahepatic inoculation of leishmania obtained from a case of oriental sore originating in Athens and that this animal is susceptible to infection with the leucocytic haemogregarine (*Hepatozoon canis*) of the dog. He promises to give further details of these experiments in a future publication.

C. M. W.

CAMINOPETROS (J.). Sur la faune des phlébotomes de la Grèce. Leur distribution dans les foyers de kala-azar. [**Phlebotomi of Greece in Relation to K.A. Foci.**]—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 450-455.

From collections of sandflies made from various parts of Greece the following five species have been found :—*papatasi*, *major*, *tobbi*, *sergenti*, *parroti*. The three first named species have been found in different parts of Greece in the houses and kennels. It is noted that it is not exceptional to capture *major* and *tobbi* in houses in the morning or some time before sunset, contrary to the claim that these are exclusively nocturnal in habit.

C. M. W.

MCCLURE (Robert B.). **Some Public Health Measures applied to Kala Azar.**—*Chinese Med. Jl.* 1934. July. Vol. 48. No. 7. pp. 659-662.

The author describes a system for the treatment of groups of kala azar cases in their own villages by technicians who are specially trained for this work. The treatment given is not free but on the basis of reduced fees for numbers treated at one time. It seems to the

author that this is a real public health measure, for the treatment of the small number of cases which come to hospital from a triangular area measuring 90 by 100 by 60 miles does little if anything to check the spread of the disease. For details of the method and its cost reference must be made to the paper itself. C. M. W.

RUIZ (Pedro Máximo). A proposito de tres casos de kala-azar infantil. [Three Cases of Infantile K.A.].—*Medicina Países Cálidos*. Madrid. 1934. Sept. Vol. 7. No. 9. pp. 429–432.

The three cases referred to are of interest in that the nature of the disease was not suspected till leishmania were discovered in the blood films. It is evident that when spleen puncture is not possible the examination of blood films, either thick or thin, may be carried out for diagnostic purposes. C. M. W.

GILKS (John L.). [Discovery of a Case of Kala Azar from the Elgeyo Reserve.] [Correspondence.].—*East African Med. J.* 1934. June. Vol. 11. No. 3. pp. 101–102.

A note on a case of kala azar in Kenya appeared in the *East African Journal* (see this *Bulletin*, Vol. 31, p. 660) where it was described as the first autochthonous case to be diagnosed in Kenya by discovery of leishmania by spleen puncture. The writer of the letter calls attention to the fact that two cases diagnosed by liver puncture had previously been reported.

Both were autochthonous cases, the one in a European administrative officer who had been stationed on the northern frontier of the colony and the other in a Somali woman from the same district. The European officer was on his first tour in Kenya and apart from service in France during the war had never been out of England till he left for service in Kenya. The two cases were noted on p. 86 of the Annual Medical Report for the year ending 31st December, 1921, Colony and Protectorate of Kenya. C. M. W.

SMITH (R. O. A.) & LAL (Chiranjī). Peri-Anal Ulceration complicating Kala-Azar.—*Indian Med. Gaz.* 1934. Sept. Vol. 69. No. 9. p. 509.

The patient was a Hindu male aged 25 years with a history of kala azar of 5 months duration. Shortly after his admission to hospital an ulcer at the side of the anus developed. It extended fairly rapidly round the anus and involved the gluteal folds on each side, in spite of the fact that neostibosan treatment for the kala azar had been commenced. As no other cause for the ulceration than the leishmania infection could be found the neostibosan treatment was intensified, a full dose of 0.3 gm. being given every day. Within 48 hours there was improvement, pain being no longer complained of. By the time the temperature had become normal the ulcer was practically healed. Ten days later a bubo developed in the right groin. This was opened and discharged pus containing *Staphylococcus aureus*. The bubo healed rapidly. The only cause suggested for this unusual ulceration was debility due possibly to venereal disease.

A case of cancrum oris in a kala azar child had appeared to be due to scurvy for a combined treatment with krysolgan, a gold compound, and plenty of vitamin C led to healing of the ulceration, the child

making a complete recovery. In a footnote it is pointed out that the routine treatment adopted by Dr. NAPIER for cancrum oris is injections of krysolgan commencing with a dose of 0.0001 gm. together with some benign mouth wash. C. M. W.

GIRAUD (P.) & VIGNE (P.). Lésions cutanées chez un enfant atteint de kala-azar. [**Skin Lesions in a Child with K.A.**].—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 655–656.

The case reported was that of a 2½ year old child in Marseilles which was suffering from kala azar and had numerous small indolent ulcers distributed about the limbs, body and head. Though leishmania were found by spleen puncture none could be detected in scrapings from the sores. That these were due to the leishmania infection appeared probable, since with successful treatment of the general condition they healed in fifteen days. C. M. W.

BRAHMACHARI (P. N.). **Annular Type of Dermal Leishmanoid.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 205–206. With 2 plates.

The case described is that of a patient who had kala azar in 1928, for which he was treated with urea stibamine and apparently cured. Six months later skin lesions began to appear. These extended till at the time of writing there were very extensive lesions on various parts of the body. The peculiar feature of the lesions was their annular character. Section of the edge of one of the lesions showed thinning of the epidermis, absence of the papillary layer and replacement of the fibrous tissue by granulation tissue in which leishmania-laden cells occur. Two photographs show the lesions on the front of the body, arms and foot.

C. M. W.

GIRAUD (Paul) & POURSIDES (Y.). Les altérations histologiques de la rate et du foie dans le kala-azar autochtone. (Étude de 12 cas personnels.) [**Histological Changes in Spleen and Liver in K.A. Twelve Cases.**].—*Arch. Méd. Gén. et Colon.* 1934. Vol. 3. No. 1. pp. 21–40. With 5 figs.

The detailed study of the spleen and liver from 12 cases of infantile kala azar has shown that as regards the histopathology several types can be recognized but that these may be regarded as stages in one pathological process. Though one part of the spleen may be more affected than another there appears to be in any one case a close parallel between the changes which have occurred in this organ and those found in the liver, so much so that it is legitimate to speak of a hepatosplenitis of kala azar. Those interested in the subject of histopathology must consult the article in the original. C. M. W.

BOGLIOLO (Luigi). Studi sulle leishmaniosi. Sulla anatomia patologica della leishmaniosi viscerale nell' uomo. [**Histopathology of K.A.**].—*Arch. Ital. Sci. Med. Colon.* 1934. Aug. 1 & Sept. 1. Vol. 15. Nos. 8 & 9. pp. 588–636; 641–697. [5 pages of refs.] English summary (4 lines).

As a result of an autopsy on a case of infantile kala azar and the detailed study of the material obtained, together with the examination

of spleen smears obtained for diagnostic purposes from another case and bone marrow smears made for the same reason from six others, the author has described the histopathology of infantile kala azar, reviewed and tabulated the conclusions of previous workers on the subject, and generally discussed and compared his own with the findings of other investigators.

C. M. W.

- i. NATTAN-LARRIER (L.) & GRIMARD-RICHARD (L.). Diagnostic des infections leishmaniennes par la formol-stibosane réaction. [**Diagnosis of Leishmaniasis by the Formol-Stibosan Reaction.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 21. pp. 492-494.
- ii. —, NOUGUÈS (S.) & GRIMARD-RICHARD (L.). Action de l'ultrafiltration sur certaines réactions des sérums leishmaniens. [**Effect of Ultrafiltration on Reactions of Leishmanial Serums.**]—*Ibid.* No. 22. pp. 585-587.
- iii. — & GRIMARD-RICHARD (L.). Action de certains composés organiques d'antimoine sur les sérums leishmaniens. [**Action of Organic Compounds of Antimony on Leishmanial Serums.**]—*Ibid.* No. 23. pp. 716-718.
- iv. —, — & NOUGUÈS (S.). Action de certains acides organiques sur les sérums leishmaniens. [**Action of Organic Acids on Leishmanial Serums.**]—*Ibid.* No. 24. pp. 802-805.
- v. — & —. Diagnostic des infections leishmaniennes par l'acidogelification du sérum. [**Diagnosis of Leishmaniasis by Acid-Gelification of Serum.**]—*Ibid.* No. 25. pp. 920-922.

i. In testing the formol-gel reaction and the antimony test in kala azar the authors have found that more reliable results are given if the two methods are combined in what they call the formol-antimony test.

To 0.5 cc. of suspected serum are added 4 drops of a 10 per cent. solution of neostibosan followed immediately by 0.5 cc. of commercial formol. In positive cases in place of the general opacity produced by formol alone there are formed large flocculi which collect into a heavy precipitate reaching nearly to the top of the liquid in the tube. It is claimed that the test will give a positive result in most cases, human and canine, of kala azar.

ii. In most cases the serum of subjects, human or animal, infected with *Leishmania donovani* is solidified and rendered opaque in a few minutes by the addition of formol at the rate of 0.5 cc. of formol to 1 cc. of serum (formol-gel reaction). It is known that in the case of syphilitic and some other sera the addition of formol produces a solidification or gelification without any loss of transparency or change in colour. It seemed possible that in the formol-gel test for kala azar two factors were involved, the one producing gelification and the other change in colour. The authors accordingly submitted sera of infected dogs to ultrafiltration. The result was that the filtered sera retained the property of becoming opaque on the addition of formol while the gelification did not occur at all or only after a period of 18 hours. These results seem to indicate that the collodion membranes used removed the gelification factor either completely or to a large extent. It was noted that the property of kala azar serum of forming a heavy flocculation on the addition of formol and neostibosan together was affected by filtration only in that the flocculate appeared finer, a result which suggests that the formol antimony reaction does not depend on the presence of two factors, as does the formol reaction alone.

iii. The authors have tested three organic antimony compounds of equal antimony content from the point of view of their capacity to replace urea stibamine or neostibosan in the antimony or formol-antimony reactions. It was found that one of these was partly satisfactory but none gave such clear results as the pentavalent compounds more usually employed. The one which gave a partial result was antimony-thiosalicylate of sodium, a trivalent compound.

iv. The addition to the serum of a normal dog of formic, lactic or acetic acid leads in 24 hours to more or less complete gelification associated with opalescence. In the case of the sera of dogs with kala azar the gelification commences directly the reagent is added or after a delay of not more than 10 minutes, and is associated with opalescence which is more marked than that occurring in normal sera after 24 hours. It would seem that the action of formol in the formol-gel test is comparable with that of the acids mentioned.

v. It seemed possible that lactic, formic or acetic acid might replace formol in the formol-gel test for kala azar. As regards canine kala azar it was found that with lactic acid or formic acid the condition of the different sera was fairly uniform after the expiry of equal intervals of time and in this respect the results appeared more uniform than those given in the formol-gel test. It did not seem likely that the lactic acid test would be of value in the diagnosis of human kala azar as normal serum was too rapidly gelified. On the other hand the reaction with normal guinea-pig serum was less rapid than with that of the dog.

C. M. W.

D'OELSNIETZ (M.) & RONCHÈSE (A. D.). Nécessité d'une technique et d'une interprétation précises de la réaction de Chopra pour le diagnostic du kala-azar. [**Technique and Interpretation of Chopra's K.A. Reaction.**—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Oct. 29. 50th Year. 3rd Ser. No. 26. pp. 1320-1321.

In the antimony test for kala azar the authors find that if on to the surface of the serum to be tested in a narrow tube is gently poured the solution of urea stibamine there forms at the surface of contact of the two liquids in the case of kala azar sera a disc of a firm consistency which retains its place in the narrow tube but in a wider one sinks to the bottom without disintegrating. A false reaction may also show a disc which, however, forms more slowly and is less dense in that it breaks up spontaneously into flocculi which sink through the liquid. In other false reactions there is formed a mere trace of precipitate which is quickly dispersed through the serum. In the authors' experience the true reaction is given only by sera of kala azar cases.

C. M. W.

AURICCHIO (L.) & CHIEFFI (A.). Una nuova sensibile e rapida sieroreazione per la diagnosi di leishmaniosi infantile. (Nota preventiva.) [**A New Sero-Reaction for the Diagnosis of K.A.**—*Pediatria.* 1934. Aug. 1. Vol. 42. No. 8. pp. 915-920. With 3 figs. English summary (4 lines).

The authors have found that the addition of 1 cc. of a 1 in 600 solution of peptonate of iron (that employed by them was Merck's, containing 5 per cent. Fe_2O_3) to 0.2 cc. of kala azar serum gives after

10 to 40 minutes incubation at 37°C. an opalescence which increases in intensity. It is stated that this reaction is specific and may be used as a diagnostic procedure.

C. M. W.

CHUNG (Huei-Lan). **Flagellation of *Leishmania donovani* in Blood from Normal and Infected Hamsters.**—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1259–1260

If a small portion of infected spleen from a kala azar hamster is ground up with heart blood from the same or a healthy animal, and hanging drop preparations are made from the material, it will be found that at a temperature of 20°C. or 22°C. flagellates will develop from the leishmania. In spite of the fact that no growth occurred at 37°C. the author suggests that the result indicates the possibility of leishmania flagellating in the mammalian host.

C. M. W.

NATTAN-LARRIER (L.) & GRIMARD-RICHARD (L.). Culture des leishmania sur le milieu N.N.N. "mouillé." [**Culture of *Leishmania* on Wetted N.N.N. Medium.**]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 656–658.

In order to increase the water of condensation in N.N.N. medium for the culture of leishmania the authors have found that after the first incubation of the freshly prepared medium at 38°C. for 24 hours 2 cc. of 0.9 per cent. sodium chloride solution can be added to each tube. The tubes are allowed to remain at 38°C. in the sloped position for a further 24 hours. This medium has given a good growth of leishmania. Furthermore it has been found that after growth has proceeded for some time in one of these tubes it is possible to remove the liquid and replace it by fresh saline solution. The tube is incubated at 38°C. for 8 to 24 hours in the sloped position, after which growth of the leishmania will recommence in the saline which has taken up sufficient haemoglobin from the solid part of the medium. The short exposure to 38°C. has not destroyed all the flagellates left in the tube. It is possible that the process might be repeated a number of times.

C. M. W.

ADLER (S.). **Culture of *Leishmanias* and Other *Trypanosomidae* in Haemoglobin-free Media.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 201–204.

In view of the statements which have been made by LWOFF, M. & A. (1933, 1934) and others that *Leptomonas ctenocephali* and *Strigomonas fasciculata* will not grow in haemoglobin-free media and that a concentration of 1 : 500 defibrinated rabbit blood is essential for continued culture of the former, the author points out that he has for many years cultivated various leishmania and trypanosomes in media in which the blood is replaced by rabbit serum (Löcke-serum agar) where only unavoidable traces of blood (often less than 1 : 5000) are present.

C. M. W.

IGLESIAS (Democrates). Leishmaniosis canina natural en Fregeneda (Salamanca). [**Canine K.A. in Salamanca.**]—*Medicina Paises Cálidos*. Madrid. 1934. Aug. Vol. 7. No. 8. pp. 370-374. [22 refs.]

The author discusses the formol-gel test for the diagnosis of canine kala azar. The application of the test to 10 dogs in Salamanca showed that these had a positive reaction. The dog giving the most marked reaction was destroyed and found to have a heavy leishmania infection.

C. M. W.

GIRAUD (Paul) & CIAUDO (P.). Absence de transmission héréditaire des caractères sérologiques de la leishmaniose interne chez le chien. [**Serological Characters of Canine K.A. not transmitted Hereditarily.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 20. pp. 433-435.

A female dog was infected with kala azar by intraperitoneal injection of spleen material from another dog. Six months later, after infection had been proved to have occurred, a litter of 10 young ones was born. The formol-gel and antimony reactions, which had been negative before the inoculation, became positive, while the albumin globulin ratio which had been 2.25 before inoculation became 0.63 a few days before the birth of the six young ones. The serum of six of these was pooled and it was found that the formol-gel and antimony reactions were negative. On the other hand the albumin-globulin ratio was 0.71. Careful examination of the organs of the six young dogs failed to reveal any leishmania infection. The authors do not regard the inversion of the albumin-globulin ratio as in any way specific for kala azar as are the other two reactions.

C. M. W.

CAMINOPETROS (J.). Lésions cutanées du chien, revêtant les caractères du bouton d'Orient. [**Oriental Sore-like Lesions in K.A. Dogs.**]—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 527-534. With 5 figs.

Attention is called to the existence in Greece of cutaneous lesions in dogs resembling oriental sore. From these leishmania can be obtained but, as has previously been noted by other observers, these lesions are merely manifestations of a generalized kala azar and are not oriental sores. The paper gives photographs of the skin lesions on three kala azar dogs.

C. M. W.

SMITH (R. O. A.), KRISHNAN (K. V.) & MUKERJI (S.). **Identification of Larvae of the Genus *Phlebotomus*.**—*Indian Jl. Med. Res.* 1934. Apr. Vol. 21. No. 4. pp. 661-667. With 2 plates.

The authors have compared the external anatomy of the larvae of *Phlebotomus argentipes*, *papatasi* and "*minutus*" (in the broad sense of the word). They find differential characters in all parts of the larva's body: the characters are in the chaetotaxy and are fully illustrated.

Larvae of *Phlebotomus* can now be found in nature by washing soil and débris through a series of graded sieves. The authors are able to identify those of *P. argentipes* and in this way define its natural breeding places.

P. A. Buxton.

KHALIL (M.). Dermal Leishmaniasis. A Study of an Endemic Focus in Egypt.—*Arch. f. Schiff- u. Trop.-Hyg.* 1934. Oct. Vol. 38. No. 10. pp. 417–433. With 11 text figs. [43 refs.]

This paper describes the endemic centre of oriental sore which was discovered in the Zagazig area about 30 to 40 miles north-east of Cairo. It has been referred to more briefly in another paper.

The subject is discussed from the epidemiological and endemiological aspects and it is concluded that, as no particular age group is more susceptible than another, the disease is of recent introduction. From the point of view of immunity it does not appear that this is absolute after one attack, for a number of people showing scars of old sores had become reinfected. It was also apparent that individuals with active sores were less liable to show malarial parasites in the blood than those without them. With reference to treatment many forms have been tried with unsatisfactory results. Surgical methods, such as thermo-cauterization, diathermy, and excision, were more reliable when they were applicable. Sandflies, chiefly *Phlebotomus papatasi*, were plentiful in the area. The endemic area lies on the camel route from Palestine and the disease has been traced all along this route from Salhia to Zagazig. Kantara, also on the route, was found by KLIGLER to be infected in 1923. C. M. W.

ROBERTS (F. W.). Cutaneous Leishmaniasis. Report of Two Cases.—*Arch. Dermat. & Syph.* 1934. Sept. Vol. 30. No. 3. pp. 401–408. With 4 figs. [20 refs.]

In both the cases reported the disease, diagnosed by discovery of *Leishmania tropica*, was contracted in the Eastern Mediterranean, though in the first case, in an Armenian youth aged 16, the first sign of the lesion was noticed on the front of the leg three months after arrival in the U.S.A. In the second case, in a girl, the disease had commenced in Palestine and was peculiar in that it finally took the form of a granulating area as large as the hand and situated behind the left shoulder. On one edge of this area was a long curved extending ulcer. A cure was effected by excision of the whole area by electrocautery, followed by skin grafting. C. M. W.

DOSTROVSKY (A.). Leishmania Recidiva of the Skin.—*Harefuah.* 1934. May–June. Vol. 8. No. 3. [In Hebrew pp. 118–124. With 1 text fig. & 4 figs. on 1 plate. English summary pp. 1–2.]

In reporting on cases of oriental sore in Palestine the author calls attention to the chronicity of the disease which is marked in some cases, one having been under observation for 6 years. The chronic lesions tend to heal at the centre and to extend slowly at the periphery where small nodules are formed on the skin surrounding the sore. These nodules in some cases form complete circles round the sore. Gradually the margin of the sore extends to absorb the nodules which generally occur in asthenic and poorly nourished subjects and in those who have received inadequate treatment. The possibility of tuberculosis of the skin or tertiary lues was considered but there was no evidence of this. The author says that the vaccine reaction and positive leishmania culture carried out by ADLER suggest a special type of leishmania which may be called "*Leishmania recidiva*." [The suggestion of a new

name for the parasite is perhaps unfortunate, as there is no evidence that the parasite is not *L. tropica*. Perhaps the author was naming the skin condition and had intended writing Leishmaniasis recidiva.]

C. M. W.

RABELLO, Jr. Structure histologique et allergie dans la leishmaniose américaine. [**Histology and Allergy in American Leishmaniasis.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 29. pp. 210-212.

The characteristic structure of the skin lesion of S. American leishmaniasis is that of an inflammatory granuloma infiltrated with epithelioid cells and a certain number of giant cells. The examination of 62 of these cases at Rio de Janeiro between 1926 and 1934 has shown that it is only in the early months of an infection that the characteristic structure is seen.

In cases of about 6 months duration about half show the specific structure and the other half that of a simple granuloma. The longer the duration of the disease the fewer are the cases with the characteristic histological structure. In this connexion it is recalled that Buss pointed out that leishmania could only be found in about half the cases. The specific lesion is not clearly defined in infections of the mucous membranes. The author considers the change in character of the lesions a protective reaction which occurs to a higher degree in the mucous membranes than in the skin; hence the fact that the skin lesions are much more common than those of the mucosae.

C. M. W.

Fox (Howard). **American Leishmaniasis. Further Observations.**—*Arch. Dermat. & Syph.* 1934. Aug. Vol. 30. No. 2. pp. 241-242.

The article is mainly written as a protest against the use of the word "espundia" in American text books instead of the more general term "muco-cutaneous leishmaniasis" of which "espundia" is merely the local Peruvian and Bolivian name. The author says it would be just as inconsistent to speak of scabies as Hongkong itch.

C. M. W.

PARROT (L.). **The Natural Transmission of Mediterranean Leishmaniasis.**—*Quart. Bull. Health Organisation, League of Nations.* Geneva. 1934. June. Vol. 3. No. 2. pp. 202-219. [89 refs.]

This is a general discussion of the possible methods of transmission of oriental sore and kala azar in the Mediterranean area. The author summarizes the available data and concludes that sandfly transmission is the most reasonable explanation of the distribution of these diseases.

C. M. W.

BOGLIOLO (Luigi). Studi sulle leishmaniosi. II. Le così dette "riserve del virus" leishmaniosico. [**The So-called Reservoirs of Leishmanial Virus.**]—*Ann. di Med. Nav. e Colon.* 1934. Sept.-Oct. 40th Year. Vol. 2. No. 3-4. pp. 534-548. [42 refs.] English summary.

After a lengthy discussion of the possible relationship of leptomnads of lizards, insects and euphorbias to kala azar and oriental sore, which are endemic in Apulia where the author works, he informs his readers that an examination of the local plants of the group referred to has given only negative results as regards the presence of flagellates.

C. M. W.

BROQUET (C.). Questions concernant la leishmaniose viscérale dans le bassin méditerranéen. [*Mediterranean K.A.*].—*Bull. Office Internat. d'Hyg. Publique*. 1934. May. Vol. 26. No. 5. pp. 893-903.

This article concerns chiefly discussions on Mediterranean kala azar which took place at the International Congress of Mediterranean Hygiene at Marseilles in 1932, and gives no new information. C. M. W.

GRECO (Zaira). Prime osservazioni statistiche e considerazioni generali sulla leishmaniosi viscerale studiata in Puglia. [*K.A. in Apulia.*].—*Ann. di Med. Nav. e Colon.* 1934. July-Aug. 40th Year. Vol. 2. No. 1-2. pp. 406-430. [47 refs.]

The paper is a detailed analysis of the data relating to 49 cases of infantile kala azar observed between 1920 and 1933 in the district of Apulia in Southern Italy. C. M. W.

GRECO (Zaira). Il primo caso di leishmaniosi viscerale infantile con pigmentazione cutanea nel bacino del Mediterraneo (vero Kala-Azar). [*Case of Infantile K.A. with Skin Pigmentation in the Mediterranean Basin.*].—*Arch. Ital. Sci. Med. Colon.* 1934. July 1. Vol. 15. No. 7. pp. 518-526. [12 refs.] English summary (4 lines).

The case of infantile kala azar discussed in the paper was in a child aged 25 months, of Southern Italy. In the author's opinion the definite pigmentation of the skin which was such a marked feature of the case serves to link the Indian and Mediterranean diseases. C. M. W.

KOSTAREVA (E.). Kala-Azar at Agdashski District of Armenia.—*Rev. Microbiol., Epidémiol. et Parasit.* 1933. Vol. 12. No. 4. [In Russian. pp. 299-300. English summary p. 301.]

It is recorded that at Agdash in Armenia during 1929-1931 the author diagnosed by spleen puncture 30 cases of kala azar chiefly, but not exclusively, in children. Instances of dermal leishmaniasis were also observed. C. M. W.

YEN (Albert C. H.) & CHUNG (Huei-Lan). Cultivation of *Leishmania donovani* in Media of Embryonic Chick Tissues.—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1258-1259.

It has been found that in sterile chick tissues in Tyrode's solution leishmania will multiply as the flagellate form at 20°C. No growth occurred at 37°C. C. M. W.

SARNELLI (Tommaso). Sul primo caso di leishmaniosi cutanea (bottone d'Oriente) autoctono dell'Italia centrale. (Seconda memoria.) [*First Case of Oriental Sore from Central Italy.*].—*Arch. Ital. Sci. Med. Colon.* 1934. Sept. 1. Vol. 15. No. 9. pp. 698-705. With 4 figs. English summary (6 lines).

The case reported in this paper had been previously described by the author as probably the first case from Central Italy, Abruzzo. The lesion on the right eyelid cleared up under treatment with neostibosan. C. M. W.

- PELI (Gino) & BENIGNETTI (Diego). Leishmaniosi cutanea autoctona nella provincia di Pesaro-Urbino. [**Oriental Sore in the Province of Pesaro-Urbino.**—*Giorn. Ital. di Malat. Esot. e Trop.* 1934. May 31. Vol. 7. No. 5. pp. 116, 119–122, 125–128. With 12 figs. [14 refs.]

A description of 5 cases of oriental sore from the Province of Pesaro on the Adriatic coast of Italy. The disease appears to be endemic in this area.

C. M. W.

- RONCONI (Luigi). La röntgenterapia nella leishmaniosi cutanea. [**X-Ray Treatment of Oriental Sore.**—*Policlino. Sez. Prat.* 1934. Sept. 24. Vol. 41. No. 38. pp. 1480–1482.

The author describes the treatment of 2 cases of oriental sore by exposure to X-rays with very satisfactory result.

C. M. W.

- DE ALDA CALLEJA (Martin). Dos historias clinicas. "Kala-azar y fiebre recurrente."—*Medicina Paises Calidos*. Madrid. 1934. Aug. Vol. 7. No. 8. pp. 375–379. With 1 chart.
- DE BONA (Giuseppe). Contributo allo studio dell'antimonio e dei suoi composti in alcune affezioni tropicali. (Kala-azar—Granuloma ulcerativo venereo—Bilharziosi.)—*Arch. Ital. Sci. Med. Colon.* 1934. Aug. 1. Vol. 15. No. 8. pp. 571–576. English summary (4 lines).
- BUTO (T.) & YAMAMOTO (Y.). Case of Kala-Azar found in a Native Child born in Niu-Chuang, Manchoukuo.—*Jl. Oriental Med.* 1934. July. Vol. 21. No. 1. [In Japanese pp. 151–156. With 1 text fig & 3 figs. on 1 plate. [14 refs.] English summary p. 12.]
- MONTAÑÉS (P.) & NEGRO (E.). Dos casos de botón de Oriente en la Región Valenciana.—*Trabajos del Sanatorio Nacional de Fontilles*. 1932–1933 Vol. 1. pp. 47–51.

MALARIA.

COVELL (G.) & BAILY (J. D.). **Malaria in Sind. Part IX. Malaria in Sukkur District. Part X. Malaria in Dadu District. Part XI. Malaria in Larkana District.**—*Records of the Malaria Survey of India*. 1934. June. Vol. 4. No. 2. pp. 119-143; 145-164; 165-191. [20 refs.]

Part IX. The subsoil water has been rising for some years and will cause an increase of malaria.

The Sukkur District is traversed by the Indus which passes through a gorge at Sukkur city. The Lloyd Barrage has been constructed at a point 3 miles below the gorge. A large part of the district consists of sandy desert, the rest is fertile alluvial plain. The average rainfall is 2 to 3 inches a year. A considerable part of the district is irrigated by canals coming from the Indus above the Lloyd Barrage. Epidemics of malaria occur about every 10 years, the last in 1929. These epidemic years are characterized by excessive monsoon rainfall. The spleen rates prior to the 1929 epidemic were 5 to 10 per cent. in areas under dry crop cultivation, 28 to 30 per cent. in areas under date palm cultivation, (where anopheles breed in the pits full of water which are dug round the bases of the trees), 25 to 30 per cent. in the area between the Indus and the flood-restriction embankments which is subject to annual flooding. Surveys made 8 to 10 months after the epidemic showed that the spleen rate was raised everywhere to 80 or 90 per cent. In one sub-district there has been a considerable rise in the subsoil water since 1924; this is attributed to increased rice cultivation. "A continuance of the present conditions will certainly lead to an increase of malaria in this area."

Part X.—The new Lloyd Barrage scheme may cause an increase of malaria.

Part of Dadu consists of hilly country, and part consists of a rich alluvial plain which lies between the hills and the Indus. The Manchar Lake lies in this plain. The whole of the drainage of the Lloyd Barrage scheme on the right bank of the Indus will be directed into this lake, which is connected with the Indus by the Aral river. The population is about 337,000. The incidence of malaria in the foothills is very slight, in striking contrast to conditions in other foothill regions and is attributed to the absence of such mosquitoes as *A. fluviatilis* (*listonii*), *A. maculatus*, and *A. minimus*. The Lloyd Barrage scheme will increase the rice-growing area by 200,000 acres; this may cause a rise in the subsoil water, followed by water-logging and an increase in malaria.

Part XI.—The Lloyd Barrage Scheme apparently caused an increase of malaria in Larkana.

The climate is very severe. The maximum temperature in July is generally above 110°F. and the minimum not below 80°. The ubiquitous canals and general submergence add moisture to the heat. The mean rainfall is only about 3 inches. The major part of the great rice tract of Sind lies in this district and it is irrigated, under the Lloyd barrage scheme, by the Central Rice Canal and its branches. The rice tract of Sind is a hyperendemic area with spleen rates ranging from 40 to 70 per cent. These figures were raised about 20 per cent. by the

1929 epidemic and, in some villages, they have not returned to the pre-endemic level. The barrage scheme came into operation in 1932, and it was followed by an increase of malaria which was probably caused by it. Whether this increase is permanent or not will depend upon the provision of efficient drainage.

W. Fletcher.

SWEET (W. C.) & RAO (B. A.). **Notes on Malaria in Mysore State. Part V. The Control of Anopheline Breeding in Bangalore City and its Cost in Mysore State.**—*Records of the Malaria Survey of India*. 1934. June. Vol. 4. No. 2. pp. 95–110. With 5 graphs.

There is not very much malaria in Bangalore; it has been dealt with by Paris green and *Gambusia*.

Bangalore is about 3,000 feet above sea level; it has a population of 172,000; the average maximum temperature is 85°F. and the average minimum 65°F. It is divided into two separate municipalities, the Civil and Military Station and the City. The spleen rate for the entire city was 23·2 in 1927, since when there has been a continuous decline, with a sharp drop between 1930 and 1931; in 1933, it was only 1·3. The parasite rate for the entire city, for the years 1931, '32, '33 was 3·8, and nearly all the infections were benign tertian. *A. culicifacies* breeds in the city tanks, and *A. stephensi* breeds in the wells; the latter mosquito was found in 80 per cent. of the house wells. The condition of the city's water supply precluded the closing of the wells. One of the authors brought a few *Gambusia affinis* from Italy in 1928. Nearly all of them died, but after they had been taken from the fountain in which they were originally placed and distributed in ponds and wells, they became acclimatized and increased to such an extent that millions are available and consignments have been shipped to various parts of India. Some of the wells have been dealt with by introducing *Gambusia*, and others by applying 2 per cent. Paris green. Tests for arsenic were positive only immediately after the application of Paris green; none was found in the water or in the deposits from wells which had been treated weekly for over a year. The Paris green treatment was the more successful, but the *Gambusia* method was cheaper and it has been adopted. The wells are restocked every 3 or 4 months. Malaria control was begun in January 1930 and was followed by a sharp drop in the spleen rate which has been maintained since. There was also a great reduction in the numbers of anopheles caught at the catching stations.

W. F.

SWEET (W. C.). **Notes on Malaria in Mysore State. Part VI. Haemoglobin and Malaria.**—*Records of the Malaria Survey of India*. 1934. June. Vol. 4. No. 2. pp. 111–117. With 1 graph.

The average haemoglobin for males was 72·2 and for females 70·9 per cent. People with malaria parasites in the blood had an average haemoglobin of 69·2; those without parasites averaged 71·8. In one village, the average haemoglobin was 67·7 before control was begun, and 77·7 three years after. "The increases and decreases in average haemoglobins were statistically significant, but there was no way of judging what this might mean for the general health of the people concerned." Tallquist's method was used.

W. F.

WINTER (H. G.). **Malaria Control in Bengal.**—*Jl. Roy. Army Med. Corps.* 1934. Oct. Vol. 63. No. 4. pp. 238-246.

The author shows how the development of the Ganges Delta has increased malaria.

Antimalaria work, in the past, was largely left to local authorities but, at the end of 1930, the Army Department of the Government of India recommended the formation of Anti-Malaria Co-operative Committees to co-ordinate the numerous schemes, and the Government of Bengal is now instituting these co-operative committees throughout the Province. In addition to the official organization, there are voluntary societies such as the Central Co-operative Anti-Malaria Society Ltd. There are over 2,000 of these voluntary societies in Bengal and the number is growing. Funds are obtained by donations and by loans from the Government. They are administered by the villagers, and most of the labour is voluntary.

The malaria of the Delta of the Ganges is largely man made. Nature's method of land-reclamation is for the rivers in the flood season, bringing up large quantities of silt, to overflow into low-lying marsh-areas where the silt is deposited, thus raising the land level. Later, this flood water re-enters the rivers, and the greater volume, increasing the velocity of flow, scours out and deepens the river bed. Population has concentrated along the rivers which are the natural traffic arteries, and as the land is low-lying, the roads and railways have been built on embankments. This has interfered with natural drainage. Man's attempts at land reclamation have been by the embankment system, which consists of raising the banks of the rivers to prevent them overflowing into the marsh-areas, and providing sluice-gates in these embankments to drain the water off such land when the rivers are at their lowest. The evil effects of this method of reclamation have been : (a) decrease in the volume of water in the rivers and consequent lessened velocity, thus causing silting up and obstruction to navigation, and eventually complete stoppage of flow ; (b) the stoppage of the natural land raising process by silt ; (c) the loss of fertility of the ground owing to absence of the manurial value of natural river silt ; (d) obstruction to natural drainage ; (e) the causation of malaria by the formation of pools in the low-lying reclaimed areas. Wherever villages have sprung up, earth has been needed for raising the land round the huts and clay has been required for making bricks. Bricks are used not only for houses, but also for building roads. To obtain earth and clay, holes have been dug, and consequently the whole country is dotted with the lakes known as tanks. These tanks are usually the only water supply for washing, bathing and drinking ; in many cases they are choked with weeds and form ideal mosquito breeding grounds.

The main sewage and storm water outlet for the city of Calcutta is the Bidyadhari River. Owing to the expansion of the city and the effect of previous land reclamation schemes this river has rapidly silted up and consequently Calcutta is constantly being flooded during the monsoon. The salt lakes to the east of the city are the result of the silting of the rivers, and in this brackish water *A. ludlowi* breeds and is constantly spreading nearer and nearer to Calcutta.

The Chief Engineer to the Department of Public Health, Mr. F. C. GRIFFIN, has evolved a plan for dealing with the problem by restoring the natural drainage of the land and improving the rivers. Dr. S. N.

SUR, Malariologist to the Government of Bengal, has made an attempt to sterilize the population by mass treatment with quinine and plasmoquine; "up to date the results have been encouraging." *W. F.*

MILNE (J. Coutts). **Observations on Malaria in Taiping.**—*Malayan Med. J.* 1934. June. Vol. 9. No. 2. pp. 31–39. With 3 charts. [11 refs.]

There appears to be no correlation between meteorological conditions and the malaria curve in Taiping.

The average annual rainfall in Taiping is 166 inches. The incidence of malaria and rainfall is not correlated. There is little variation in relative humidity or temperature throughout the year. The monthly incidence of malaria, over a period of 6 years, shows an increase in May and June which is associated with an increase in *A. maculatus*—the "maculatus wave" of WATSON. There is a second small increase of malaria in October, possibly due to protracted incubation of infections acquired during the first period. Subtertian malaria causes more severe symptoms than benign tertian and consequently subtertian malaria is commoner in the hospitals of the Malay States. In 1932 out of 11,787 patients, 65.5 per cent. were subtertian and 27.08 per cent. benign tertian. Outside the hospitals, the incidence of the two types is almost equal; quartan is rare. The benign tertian curve has its maximum rise in September. *W. F.*

HELFFERICH (W. M. G.). **Merkwaardige uitkomsten van een malaria-onderzoek in de Onderafdeeling Dairilanden (Residentie Tapanoei).** [**Results of a Malaria Investigation in the Dairilands Subdivision.**]—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Oct. 23. Vol. 74. No. 22. pp. 1438–1446.

The chief result of this investigation in Sumatra was the unusual finding that the parasite index was often much higher than the spleen index and that this condition was a permanent one.

It is only in recent years that the Dairilands district has been easily accessible. The climate is a typical hill climate (altitude of 700–1,200 metres) with wide variation of day and night temperature and a heavy rainfall (3,000 mm.). Malaria is rife and appears to be a true chronic endemic malaria without any seasonal prevalence. An example of its prevalence is furnished from the garrison of the capital—58 cases in 1933 for an average strength of 56, 38 cases in women and children with average strength of 93, and 9 cases among prisoners with average strength of 9. In type the malaria was benign, mainly tertian, with only one or two days fever and little effect upon health. The carrier was probably a zoophile type or at least an out-of-doors mosquito. Thus although an energetic search was made at evening the results were always disappointing and only 43 were caught in houses, of which 29 were *A. maculatus*. On the contrary the catch in cow and buffalo stables was 842 for the same period of time and in this number were included 490 *A. maculatus* and 251 *A. fuliginosus typicus*. On several occasions parasite and spleen indices were taken and the blood smears examined at the official laboratory. These gave a low spleen index with a high, often much higher, parasite index. In the later examinations all age groups were represented, small children, school

children and adults. The general result differed, then, from that propounded for a chronic endemic malaria by SCHÜFFNER and SWELLEN-GREBEL, which should show a high spleen index in all age groups, and a much lower parasite index becoming steadily lower from the child to the adult. In the present case no parasite immunity with age can be invoked because the condition was identical in children and adults. It seems to the author that the condition in the area under investigation must point to a low virulence of the malaria parasite and a tendency to commensalism, while these features again may be associated with height above sea level. The possibility of a strain resistant to medication may also be taken into consideration. *W. F. Harvey.*

- RUSSELL (Paul F.). **Malaria and Culexidae in the Philippine Islands : History and Critical Bibliography, 1898 to 1933.**—*Philippine Is. Dept. of Agric. & Commerce, Manila, Tech. Bull. No. 1.* 1934. June 23. 115 pp. With 3 text figs. & 8 plates (2 maps).
 —. **A Neglected Early Reference to the Malaria Vector in the Philippines.**—*Amer. J. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 339-342. [10 refs.]

Malaria cannot be reduced without anti-larval control. Most of the facts given in this compilation have already been published in articles which have been summarized in this *Bulletin*.

The paper was prepared as a part of the program of Malaria Investigations, Bureau of Science, Manila, of which the author is chief, and which is jointly supported by the Bureau and by the International Health Division of the Rockefeller Foundation. The study is limited to the years 1898-1933, which constitute the American epoch in the islands. Up to that time, research studies in tropical medicine had been practically nonexistent, microscopes were rare, and nothing was known about the mosquitoes. It appears that malaria was indigenous when Magellan came in 1521, but that it was rarely as deadly as in Java or the Malay Peninsula. From 1898 until 1903, the admission rates for malaria among American white troops were between 450 and 750 per mille; from 1904 to 1908 they were between 200 and 300; from 1909 to 1913, they were between 86 and 186; from 1924 to 1928 they were between 13 and 32. Improved mosquito nets and the strictness with which their use was enforced appear to have been important factors in this reduction of malaria in the army. "From Lippincott, first to advocate nets as a protection against malaria, and Whitmore first to incriminate the stream-breeding anopheles, to the present excellent malaria-control programme at Fort Stotzenburg, the Army's record has been one of outstanding achievement." WHITMORE in 1904 found 30 per cent. of the stream-breeding "*Myzomyia funesta*" (? *minimus*) infected with malaria. Before this it was supposed that all malaria-carrying anopheles bred in swamps. MANALANG considers that the local *minimus* is identical with *A. funestus* but, according to KING, the *funestus-minimus* subgroup of the Philippines is made up of (1) *A. filipinae* Manalang 1930, (2) *A. mangyanus* Banks 1906, (3) *A. minimus* Ludlow.

In 1913, arrangements were made for the sale of quinine at a very low rate, it was also distributed free of charge, but, in 1915, after millions of tablets had been distributed, the Health Service reported that it had been a failure. MANALANG, however, still advocates "quinization or, better still, the use of plasmoquine compounds"

because he considers Paris green ineffective. The author does not agree with this opinion, "all available evidence indicates that drug control of malaria is as impossible from a practical standpoint in the Philippines as elsewhere. Moreover, it is very expensive, not only in the cost of drugs but also in salaries of those who must distribute it dose by dose. . . . But in many places throughout the Islands, Paris green control is thoroughly feasible. . . . In Calauan between 1924 and 1926, . . . the reduction in hospital costs alone was ten times greater than the actual cost of malaria control by Paris green. . . . Mosquito nets, therapeutic drugs (that is, quinine, chinoplasmin, and atabrine), and an attack on the larvae of the *funestus-minimus* subgroup will gradually subdue this disease in the Philippines. There is no evidence that without larval control malaria rates can be lowered much below their present level in these Islands. Paris green is the cheapest and most effective larvicide." The following insecticide spray has been found most useful; mix together and shake frequently 60 grs. of fresh powdered pyrethrum and 120 cc. of chloroform, filter through a Buchner funnel and add 1,000 cc. kerosene to the filtrate. "There is no evidence at all that bats, larvivoracious fish, clover, *Chara*, or cannibalistic larvae have had or could have any virtue in the control of malaria in the Philippines." Keys for the identification of the adults and larvae of the Philippine anopheles are published with this paper in the form of two large charts. W. F.

LAUREL (Alberto G.). **Feeding Activities of Some Philippine Anopheles.**—Reprinted from *Rev. Filipina Med. y Farmacia*. 1934. July. Vol. 25. No. 7. pp. 286-297. [34 refs.]

The results of precipitin tests performed on Philippine anopheles.

A. minimus enters houses to feed, but never remains there during the day. The author does not think that there are separate androphilous and zoophilous strains of *A. minimus*. "More likely our *minimus* consists of a mixed strain, and while it is generally inclined to feed on man it will also feed on animals when accessible." *A. maculatus* feeds chiefly on animals; of 338 caught during the daytime, 4 were positive for human blood and 241 for cattle blood (see EJERCITO below). Examinations of fresh-water breeding *ludlowi* showed positive reactions for cattle blood, but not for human. Salt water *ludlowi*, on the other hand, showed avidity for human blood, but they do not transmit malaria in the Philippines. W. F.

EJERCITO (Antonio). **Anopheles maculatus Theobald, Another Malaria Vector in the Philippines.**—*Jl. Philippine Islands Med. Assoc.* 1934. Sept. Vol. 14. No. 9. pp. 342-346.

A. maculatus, in the Philippines, is zoophilous, and unimportant in comparison with *A. minimus*. [See LAUREL above.]

A. maculatus is not so widely distributed in the Philippines as *A. minimus*. In some places where precipitin tests were made, it was found that over 98 per cent. of the *A. maculatus* had fed on cow's blood and only about 2 per cent. on human blood. At Bagiuo, 4,300 feet above sea level, *A. maculatus* is plentiful but there is no malarial transmission. The natural infection rate of *A. maculatus* is 0.3 per cent. The experimental infection rate is 5.26 per cent. It is much less important than *A. minimus* as a transmitter of malaria in the Philippines. W. F.

ROBERTSON (R. C.) & HU (Stephen M. K.) with Illustrations by R. V. DENT. **Mosquito Control. An Entomological Field Research Station for Mosquito Study in the Shanghai District.**—Reprinted from *China Jl.* 1934. June. Vol. 20. No. 6. pp. 344–356. With 1 map, 16 figs. on 8 plates & 1 diagram.

This is an account of the work done at the Kaochiau Field Laboratory written for the general public of Shanghai.

"The object of this paper is to place the main facts regarding the prevalence of disease-carrying mosquitoes in the Shanghai area before the general public. . . . Is the risk of contracting malaria serious in Shanghai or not?" A field laboratory was established at Kaochiau in the spring of 1933 as a branch of the Entomological Research of the Henry Lester Institute, and the greater part of this paper consists of a description of the work which is done there. It is illustrated by excellent photographs of the resting places of adult mosquitoes, and of the methods of catching them. *A. hyrcanus* Pallas var. *sinensis* Wiedemann was the only anopheline found. W. F.

PARSA (Seyfolah). Contribution à l'étude du paludisme en Perse. [**Malaria in Persia.**—44 pp. [38 refs.] 1933. Paris: Les Éditions Vêga, 43 rue Madame.

Malaria is widespread in Persia, but no organized attempt to control it has ever been undertaken.

After the capture of Khoram-Abad, in Luristan, from the insurgents, epidemics of disease, especially malaria, were so severe that military undertakings were held up for a period of six months. The surrounding country was peopled by nomads living on the verge of starvation in conditions of filth and squalor. The town itself was grossly insanitary, and was little more than a heap of ruins owing to the frequent attacks of tribesmen bent on loot. The measures undertaken were the treatment of the sick, both civil and military, and quinine prophylaxis. In addition, the government made a road connecting two important centres which passed through Khoram-Abad. The making of this road gave work to the nomad tribes, and efforts are being made to induce them to abandon their wandering life and to settle on the land bordering this road, where they can be looked after and lead a more sanitary life.

W. F.

COLLIGNON (E.). Observations sur la lutte antipaludique en 1933 dans le département d'Alger. [**Anti-Malaria Work in Algeria, 1933.**—*Arch. Inst. Pasteur d'Algérie.* 1934. June. Vol. 12. No. 2. pp. 209–226. With 14 figs. on 7 plates.

AMBIALET (R.). Observations générales sur la campagne antipaludique de 1933 dans le département de Constantine.—*Ibid.* pp. 227–246. With 2 graphs & 10 figs. on 5 plates.

GOUGET (R.). La campagne antipaludique de 1933 dans le département d'Oran.—*Ibid.* pp. 247–254. With 6 figs. on 3 plates.

Quinine appears to be the main weapon in prevention.

The principal anophelines of Algeria are *A. maculipennis*, *A. marteri* and *A. hispaniola*. *A. maculipennis* breeds in pools found in river beds, in irrigation channels, ditches, and casual collections of water. It is the anopheline of the plains and alluvial valleys. The water

in which it breeds is sweet or slightly salt, lying on a muddy bottom, stagnant or slowly moving, and with abundant vegetation. Breeding is at its height in spring. This anopheline is the most important vector in the country. *A. marteri* is found in clear water without vegetation, in the pools of mountain streams with rocky or sandy bottoms. The streams dry up in May and this species disappears. *A. hispaniola* breeds in the summer, in the streams of upland valleys containing green algae. It does not appear to be important as a vector of malaria. Anti-malaria work has been based upon the quinine prophylaxis of native children and anti-larval operations. All native children under the age of 15 are given quinine from the beginning of May until the end of November. The younger ones are given capsules, chocolate covered pills, or aristoquine (tasteless carbonic ester of quinine). The drug is well taken and, in very malarious villages, it produces an extraordinary change in the appearance of the children in the course of a few weeks. The parents are most grateful to the doctors. The quinine does not get rid of the infection, but it does get rid of the danger; it saves the lives of the children until they reach a condition of premunition, which is the goal to be aimed at with natives in a malarious country. The antilarval measures which were on a 2 kilometre radius round settlements, consisted of drainage, clearing, oiling and the introduction of gambusia.

W. F.

VAN NITSSEN (R.). Les indices endémiques palustres à Panda. [**Malaria Endemic Index at Panda, Katanga.**—*Bull. Méd. du Katanga*. 1933. Vol. 10. No. 5. pp. 127, 129, 131, 133, 135, 137.

An example of high endemicity with very little illness from malaria.

The parasitic index reaches its highest point, 96 per cent., in children between 3 and 4 years of age. The maximum gametocyte index, 55 per cent., is reached between 2 and 3. The maximum splenic index, 45 per cent., is found between the ages of 4 and 5. Most of the infections are subtertian. In spite of this high endemicity, there is little illness and the mortality is low. The labourers and their children are well nourished. Natives of Ruanda who have emigrated to Katanga show a greater sensibility to malaria than the other tribes of the Congo, and it is interesting to find that this susceptibility appears to be transmitted to their children who are born in Katanga.

W. F.

VINCKE (I.) & HENRARD (C.). Note sur la lutte antipaludique à Léopoldville. [**The Antimalaria Campaign at Leopoldville.**—*Ann Soc. Belge de Méd. Trop.* 1934. June 30. Vol. 14. No. 2. pp. 203-217.

A. gambiae, the important carrier, breeds in collections of rain water during the wet weather and in the rivers all the year round.

A. gambiae is the commonest species of anopheles in Leopoldville, and it is also the most important carrier. During the wet weather it breeds in the pools of rain water which collect in holes and depressions, many of them made by man. It breeds all the year round in the river Congo and in the streams which run into it; in the dry weather when temporary collections have disappeared, it breeds in the pools left in the

beds of the sinking rivers. The average infective index of this mosquito throughout the year was 8·6 per cent. ; it rose as high as 21·4 per cent. during the January rains ; and in the dry, cold weather of June and July it fell to 2·6. In July, the low temperature appeared to have retarded the development of the parasites for no gland infections were found. Another carrier, but one of far less importance, is *A. moucheleti*. Many other species occur in Leopoldville ; *A. nili*, *A. funestus* and *A. rufipes* though they are carriers, are very rare, and *A. mauritanus* though common, does not appear to be a carrier. W. F.

HOFFMANN (Carlos C.). Contribución al conocimiento del paludismo en la península de Yucatán. [*Malaria in Yucatán.*] Reprinted from *Bol. Inst. de Higiene*. 1934. 2nd Ser. Vol. 2. No. 1. 57 pp. With 29 figs. (2 coloured maps).

This monograph gives a clear and succinct account of malaria in the Peninsula of Yucatán. The author, who is head of the Department of Parasitology at the Institute of Hygiene, briefly describes the geography and the factors influencing the development of anopheles in the peninsula, with accompanying maps and photographs of breeding sites and charts of the rainfall from 1923 onwards.

Five species of Anopheles are found, namely, *A. albimanus*, *A. pseudo-punctipennis*, *A. crucians*, *A. vestitipennis* and *A. punctimacula* ; the first is the most dangerous. Each is described in detail together with its favourite haunts, and a diagnostic key is appended.

Then follow remarks on the prevalence of infection on certain estates, these are mainly of local interest but an instance or two may be given. On one estate 60 persons were examined and 59 had enlarged spleen, in 20 it was just palpable, and in one only was it very large. Parasites were found in four only among the 60—three among 21 children and one among 39 adults. Elsewhere, among 83 re-examined after the 1927 epidemic 46 had enlarged spleens and 62 showed parasites. *P. falciparum* was found in 53, *P. vivax* in 26, *P. malariae* in 9 ; *P. falciparum* and *P. vivax* together in 17. The epidemic had been a severe one. In November, 1,916 patients were treated, in December 2,405 and in January 2,272, or 6,593 in the three months. The usual measures were undertaken—destruction of mosquitoes, elimination of breeding sites, etc. H. H. S.

MARTINI & ZOTTA. Races d'*A. maculipennis* en Roumanie. Rapport sur un voyage d'étude effectué à travers la Roumanie pendant les mois d'août et de septembre 1933. (Sous les auspices de l'Organisation d'Hygiène de la Société des Nations.) [*A Study Tour in Rumania during August and September 1933. Races of A. maculipennis.*]—*Arch. Roumaines Path. Expér. et Microbiol.* Paris. 1934. June. Vol. 7. No. 2. pp. 135–209. With 6 figs., 6 charts & 2 maps.

The main object of this tour was to study the distribution of the different races of *A. maculipennis* and to determine the relation of this distribution to the prevalence of malaria.

The authors found that the situation resembled almost exactly that obtaining in Germany. *A. messeae* was found to be the mosquito of the broad sweet-water regions, lakes, and rivers. *A. atroparvus* was particularly common in the salt-water lakes and ponds which lie just

at the back of the shore, and are separated from the sea by banks of sand and narrow tongues of land. This mosquito is also found in collections of brackish water in the interior. *A. maculipennis maculipennis* constitutes a large proportion of the mosquitoes of the higher regions and it is sometimes found mixed with *A. messeae* or *A. atroparvus*. In the neighbourhood of Constantza, there are several coastal lakes which are separated from the Black Sea by a strip of sand. These lakes appear to be similar to one another in every way except that some of them contain sweet water while the others are brackish. The anopheline fauna differ sharply, *A. messeae* breeds in the sweet water lakes, while *A. atroparvus* is the predominant anopheline in the salt lakes. Along the shores of the Black Sea, *A. elutus* is sometimes found. *A. labranchiae* was not found by the authors in Rumania.

Much of the delta of the Danube consists of the "Plaur," which is composed of layers of tangled roots, rushes and the like, with water flowing underneath. In many places the Plaur is so thick that cattle wander over it; in other places, it is spongy and quaking. There are swarms of mosquitoes in the delta and the cattle come home at night to crowd round a fire in the village. In spite of this, there is very little malaria. The authors ascribe this absence of malaria to three causes: (1) abundant food for the population, (2) large herds of cattle, (3) the use of mosquito-nets and other methods of protection against mosquitoes. The most dangerous race of *A. maculipennis* appears to be *A. elutus*. A village which was annihilated by malaria was found to be situated near breeding grounds of this mosquito. The regions where *A. atroparvus* was prevalent were only a little less malarious. There was little malaria in the *A. messeae* regions and least of all in the places where *A. maculipennis maculipennis* flourished. The authors state, however, that under unfavourable conditions and in the absence of screening, widespread infection with benign tertian, and some cases with subtertian, may occur, even in places where the only variety is *A. messeae*. They were not able to find in Rumania examples of subtertian malaria decimating the population in regions where only *atroparvus*, *messeae* and *maculipennis* were found. The grave epidemic which occurred in the delta of the Danube, after the war, showed that this area was not free from serious malaria under all circumstances. This post-war epidemic was principally due to the destruction of the cattle by the troops, and to the consequent absence of deviation of the mosquitoes from man.

W. F.

ILVENTO (A.). **The Reclamation of the Pontine Marshes.**—*Quart. Bull. Health Organisation, League of Nations.* Geneva. 1934. June. Vol. 3. No. 2. pp. 157–201. With 18 figs. & 1 map.

"In 1926, the great 'back to the land' movement was initiated by the Duce. . . . In the Mussolini Act of December 24th 1928 . . . large areas were to be comprehensively reclaimed at a cost of 7,000 million lire."

The first part of this article is concerned with the geography and history of the Pontine Marshes, and with the attempts to colonize it which have been made for hundreds of years (see CELLI, this *Bulletin*, Vol. 31, p. 220). The author then describes the resolute way in which the problem has been attacked, and how the difficulties have been overcome.

The basic survey which forms the foundation of the present drainage work in the Pontine region was made in 1918 by officials of the Office of Works. A start was made in 1924, by the end of 1933 all natural water-courses had been regulated, and throughout almost the whole region floods and stagnant pools were eliminated. The owners of the land hesitated to sink much capital in the inauguration of new farming methods and in building new houses; consequently the Duce called upon the National Ex-Servicemen's Association to carry out the program of agricultural land-improvement and re-population of the zone. This association provided considerable funds "and a still greater asset in the persons of technical experts of long experience." In 1931, 18,000 hectares of land were given to the Association. The canalization of the upper waters was already completed and these were collected into the great Mussolini drainage canal and led down to the sea. The land was divided into holdings, 515 farm-houses were built, and the peasants were instructed in rational farming methods so that each family might become the owner of its farm within the time-limit of one year. "Each farm-building includes a dwelling-house built on a damp-course and comprising a ground-floor kitchen and storeroom and one upper storey with three to five bedrooms and living-rooms, the doors and windows screened against flies and mosquitoes; a stable for 8 to 10 head of livestock...; a chicken-run and pigsty; a well of fresh water for domestic use; a cesspool and a manure-heap.... The National Association bears the cost of preparing the soil of each farm, of buildings, live and dead stock, and the farm-tracks.... The farm is handed over to the peasant immediately all this work has been completed."



Workers' Hutment Village erected by the National Ex-Servicemen's Association to house the workmen engaged in preparing the peasants' farms in the Agro Pontino.

[Reproduced from the *Quarterly Bulletin of the Health Organisation, League of Nations.*]

An army of workmen was employed. At first they were taken to their work daily in motor-coaches, but later, collections of screened huts, or barracks, were constructed (as shown in the photograph) for groups of 500 to 2,000 workmen, where their health was properly looked after, and their happiness and recreation cared for. Then came the peasants, and soon a town grew up. In December 1932, the Commune of Littoria was officially constituted. The square in the centre of the town was formerly one of the most malaria-ridden spots in the region. The Duce declared in his speech delivered at the inauguration of the Commune, "This is a red-letter day in the history of *Agro Pontino*. It is a day of triumph for the whole nation. What 25 centuries attempted in vain we now see accomplished before our eyes. . . . On October 28th, 1933, we shall inaugurate 981 new homes for settlers; on April 21st, 1934, we shall inaugurate the new Commune of Sabaudia, and on October 28th, 1934, the third Commune—Pontinia. . . . Formerly, to find work we had to pass the Alps or cross the ocean. Now the land is at our doors, within half-an-hour of Rome."

The number of persons resident in the *Agro Pontino* was 1,800 in July 1924, 12,000 in July 1932, 40,430 in July 1933. In 1933, all health services were placed under the Italian Red Cross. Quinine prophylaxis is chiefly used for persons not permanently resident in the territory. It always prevents fever and pernicious malaria, and is therefore in great favour. Under the present conditions of concentration, malaria can be diagnosed early and the patients can be treated in the new local hospitals. Carriers of infection are followed up and treated. Adult anopheles are destroyed in the houses with paraffin atomizers, smoke bombs and the like. The increase of cattle has deviated anopheles in some areas, and drainage, oiling and Paris green have lessened their numbers. The antimosquito squads carry out the latter measures for a radius of 1,000 metres (0.625 miles) round all dwellings. In 1933, though the number of people exposed to infection had trebled, the morbidity rate fell to 2.09 per cent., and the death rate to 0.34 per thousand.

On August 4th 1933, the Duce inaugurated a seaside colony at Torre Olevola for the children of the Littoria settlers. This place—3 kilometres from Terracina—was formerly well known for its amazing marsh landscape of dead waters and gigantic water-lilies, and was completely in the grip of malaria. "The children immensely enjoyed their life in the colony; a number of malaria cases were cured, and no new cases occurred." The author concludes that there are only two achievements which "can be approximated to the new civilized life in the malarial lands of Italy . . . the reclamation of the Panama Canal Zone and the draining of the Zuider Zee." W. F.

VERSLAGEN EN MEDEDEELINGEN BETREFFENDE DE VOLKSGEZONDHEID. 1934. June. 36 pp. With 2 figs.—Verslag over de jaren 1932 en 1933 van de malaria-comissie uit den gezondheidsraad. [Report for 1932 and 1933 of the Malaria Commission of the Sanitary Board.]

This commission in its several reports represents the facts and figures, with their analysis, of the campaign against malaria in Holland. The chief malaria station was at Medemblik and much useful information has been collected, especially on the subjects of the value of an anti-larval campaign, the first three years of land reclamation of the

Wieringermeer area and attempts at finding a suitable cheap and efficient insecticide for use in houses.

The antilarval campaign in Medemblik during the years 1927 to 1931 was successful in reducing anopheles to a figure 4 to 5 times as low as that in the area outside the field of operations. With the termination of the operations the anopheles density rose in 1932 and 1933 to a much higher level in Medemblik than before. The campaign, then, had produced its effect and yet it was found insufficient completely to prevent the rise in malaria between 1929 and 1931. When the cost of the procedure, at one florin per inhabitant, is taken into account the conclusion is irresistible that large scale operations are inadvisable in a watery land like Holland where malaria is of benign type.

Observations in the reclaimed area of Wieringermeer are very interesting. Here most of the ditches were too salt to serve as breeding places and in the polder the density of mosquitoes, determined from the mosquito population of the test stables, at a distance of 3, 5 and 10 kilometres from the old land was in 1932 one quarter of the density of those in the corresponding stables at Medemblik, which by that time was no longer protected by antilarval measures. But the natural method of protection in the Wieringermeer polder was able to effect nothing better than the artificial in Medemblik. An important observation made in the Wieringermeer area was as to the distance of flight of mosquitoes, which was shown could be to 9 and 14 kilometres. This question of distance is supposed to have a bearing upon the value or want of value of antilarval measures in a given area, when that area is surrounded by others in which no measures are taken. When, however, the point was put to actual test, as it was for the 3-kilometre long village Wormerveer with an epidemic of malaria in the northern kilometre, it was found that no indication of spread of malaria to the middle and southerly portions was forthcoming. Was this due to the fact that infected mosquitoes, which are sick mosquitoes, cannot fly far or was it that mosquitoes generally do not really fly to any great distance? The latter supposition seems the more probable. Mosquitoes fly little, rest in houses and at the most find their way only into an adjacent house. Thus an argument is found for the utility, on a small scale at least, of antilarval measures in spite of the contrary experience at Medemblik and Wieringermeer.

An active search was made for a spray insecticide, as this is regarded as a most useful antimalarial measure for dwelling houses. The formula arrived at for use in dwelling houses was:—petroleum 1,000 cc.; pyrethrum extract 5 gm.; sassafras oil 5 cc.; methyl-salicylate 20 cc.; and for stables:—petroleum 550 cc.; vaseline oil 450 cc.; pyrethrum extract 10 gm.; sassafras oil 10 cc.; methyl-salicylate 20 cc.

Other questions which received attention were the bearing of races of *Anopheles maculipennis*, small type and large type, upon malaria; the separation of *Plasmodium vivax* into races, as exemplified by the Madagascar and the Dutch races; the treatment of tertian malaria with plasmoquine and Henry's diagnostic serum reaction. *W. F. Harvey.*

SOUTHERN MEDICAL JOURNAL. 1934. May, June & July. Vol. 27. Nos. 5, 6 & 7. pp. 448-466; 546-561; 642-657. **Symposium on Malaria. Parts 1, 2 & 3.** [19 papers.]

The Chairman, Dr. C. F. CRAIG, opened the Symposium with an address on certain unsolved problems in malaria. He drew special

attention to the following :—(1) The species of malaria plasmodia : JAMES, NICOL and SHUTE have shown that *P. ovale* is a valid species, and further research may show that there are yet others. He stated that *P. ovale* was first described by himself in 1900 ; but it was not named until 1922 when STEPHENS observed it. (2) The morphological identity of some of the malaria parasites of apes and monkeys with those of man, and the successful transmission of monkey malaria to man by KNOWLES and Das GUPTA, emphasizes the necessity for further study of the relationship of the plasmodia of man and monkeys. (3) Perhaps the most important of the unsolved problems concerns the cause of long term relapses, and the origin of gametocytes. (4) It has recently been shown that other genera than *Aedes* can transmit yellow fever. Much more work is necessary before we can be sure that anopheline mosquitoes are the only transmitters of malarial infections. (5) The unusually rapid spread of malaria in some epidemics has been very difficult to understand, and it is possible that mechanical transmission by mosquitoes or other biting insects sometimes occurs, as it occurs in trypanosomiasis and dengue fever. (6) The study of immunity in malaria offers a wide field for research.

Drs. G. E. RILEY, E. C. FAUST, and T. H. D. GRIFFITTS, gave a survey of recent work in the epidemiology of malaria. They dealt with the work of GIGLIOLI in British Guiana, with the study of the different races of *A. maculipennis* in Europe, with the investigation of monkey malaria in India, and with work in other parts of the world which has been summarized in this *Bulletin*. Drs. E. C. FAUST and C. F. DIBOLL have compiled the death rates due to malaria in the 14 southern States. The rate was 8 per 100,000 in 1925, it rose gradually to 11·4 in 1928, and has since declined to 6·8 in 1932. The 1933 figures, which are not yet complete, indicate that the rate is rising again.

Dr. E. H. HINMAN contributed some interesting observations on the hibernation of *A. quadrimaculatus*. It is generally accepted that this species is active throughout the winter, but at Fort Jackson in an abandoned fort on the west bank of the Mississippi, 65 miles below New Orleans, Dr. Hinman found that vast numbers collected for shelter. Behind the fort there are wide stretches of salt marsh where *A. crucians* and *A. atropos* breed, but not *A. quadrimaculatus*. In the summer, a few *A. quadrimaculatus* were found in the fort, but in November there were millions ; some rooms contained more than 10,000. In December they were even more numerous. In January and February there was a considerable reduction in the numbers, and in the latter part of March it was difficult to find any specimens. A similar sheltering or hibernation of *A. quadrimaculatus* has been found nowhere else. The mosquitoes breeding in the adjacent salt marsh belonged to other species, and did not shelter in the fort ; the *A. quadrimaculatus* apparently came from distant breeding places.

Dr. T. H. D. GRIFFITTS examined the blood of children in 79 white schools and 57 negro schools in Florida. Parasites were present in 3·8 per cent. of the white children and 9·7 of the black children. Of the infections in white children, 47 per cent. were due to *P. falciparum* and 30 per cent. to *P. vivax* ; in black children the proportion was *P. falciparum* 62, and *P. vivax* 23 per cent.

Dr. K. DRENSKY and Dr. R. K. COLLINS recorded the interesting results of their observations on the winter infection rates in *A. maculipennis* and *A. superpictus* in Bu-¹ ² ³ ⁴ ⁵ ⁶ ⁷ ⁸ ⁹ ¹⁰ ¹¹ ¹² ¹³ ¹⁴ ¹⁵ ¹⁶ ¹⁷ ¹⁸ ¹⁹ ²⁰ ²¹ ²² ²³ ²⁴ ²⁵ ²⁶ ²⁷ ²⁸ ²⁹ ³⁰ ³¹ ³² ³³ ³⁴ ³⁵ ³⁶ ³⁷ ³⁸ ³⁹ ⁴⁰ ⁴¹ ⁴² ⁴³ ⁴⁴ ⁴⁵ ⁴⁶ ⁴⁷ ⁴⁸ ⁴⁹ ⁵⁰ ⁵¹ ⁵² ⁵³ ⁵⁴ ⁵⁵ ⁵⁶ ⁵⁷ ⁵⁸ ⁵⁹ ⁶⁰ ⁶¹ ⁶² ⁶³ ⁶⁴ ⁶⁵ ⁶⁶ ⁶⁷ ⁶⁸ ⁶⁹ ⁷⁰ ⁷¹ ⁷² ⁷³ ⁷⁴ ⁷⁵ ⁷⁶ ⁷⁷ ⁷⁸ ⁷⁹ ⁸⁰ ⁸¹ ⁸² ⁸³ ⁸⁴ ⁸⁵ ⁸⁶ ⁸⁷ ⁸⁸ ⁸⁹ ⁹⁰ ⁹¹ ⁹² ⁹³ ⁹⁴ ⁹⁵ ⁹⁶ ⁹⁷ ⁹⁸ ⁹⁹ ¹⁰⁰ ¹⁰¹ ¹⁰² ¹⁰³ ¹⁰⁴ ¹⁰⁵ ¹⁰⁶ ¹⁰⁷ ¹⁰⁸ ¹⁰⁹ ¹¹⁰ ¹¹¹ ¹¹² ¹¹³ ¹¹⁴ ¹¹⁵ ¹¹⁶ ¹¹⁷ ¹¹⁸ ¹¹⁹ ¹²⁰ ¹²¹ ¹²² ¹²³ ¹²⁴ ¹²⁵ ¹²⁶ ¹²⁷ ¹²⁸ ¹²⁹ ¹³⁰ ¹³¹ ¹³² ¹³³ ¹³⁴ ¹³⁵ ¹³⁶ ¹³⁷ ¹³⁸ ¹³⁹ ¹⁴⁰ ¹⁴¹ ¹⁴² ¹⁴³ ¹⁴⁴ ¹⁴⁵ ¹⁴⁶ ¹⁴⁷ ¹⁴⁸ ¹⁴⁹ ¹⁵⁰ ¹⁵¹ ¹⁵² ¹⁵³ ¹⁵⁴ ¹⁵⁵ ¹⁵⁶ ¹⁵⁷ ¹⁵⁸ ¹⁵⁹ ¹⁶⁰ ¹⁶¹ ¹⁶² ¹⁶³ ¹⁶⁴ ¹⁶⁵ ¹⁶⁶ ¹⁶⁷ ¹⁶⁸ ¹⁶⁹ ¹⁷⁰ ¹⁷¹ ¹⁷² ¹⁷³ ¹⁷⁴ ¹⁷⁵ ¹⁷⁶ ¹⁷⁷ ¹⁷⁸ ¹⁷⁹ ¹⁸⁰ ¹⁸¹ ¹⁸² ¹⁸³ ¹⁸⁴ ¹⁸⁵ ¹⁸⁶ ¹⁸⁷ ¹⁸⁸ ¹⁸⁹ ¹⁹⁰ ¹⁹¹ ¹⁹² ¹⁹³ ¹⁹⁴ ¹⁹⁵ ¹⁹⁶ ¹⁹⁷ ¹⁹⁸ ¹⁹⁹ ²⁰⁰ ²⁰¹ ²⁰² ²⁰³ ²⁰⁴ ²⁰⁵ ²⁰⁶ ²⁰⁷ ²⁰⁸ ²⁰⁹ ²¹⁰ ²¹¹ ²¹² ²¹³ ²¹⁴ ²¹⁵ ²¹⁶ ²¹⁷ ²¹⁸ ²¹⁹ ²²⁰ ²²¹ ²²² ²²³ ²²⁴ ²²⁵ ²²⁶ ²²⁷ ²²⁸ ²²⁹ ²³⁰ ²³¹ ²³² ²³³ ²³⁴ ²³⁵ ²³⁶ ²³⁷ ²³⁸ ²³⁹ ²⁴⁰ ²⁴¹ ²⁴² 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in Holland, and WENYON in Macedonia, have found infections among hibernating mosquitoes. It has been shown experimentally that low temperatures retard the development of the parasite in the mosquito, but they do not kill it, and with the return of warm weather development proceeds anew. It is common knowledge that in certain parts of Bulgaria it is not unusual for babies born in the winter to suffer from malaria in the spring. The authors dissected a number of *A. maculipennis* and *A. superpictus* caught in the Petritch district of Bulgaria between February 7 and April 20, 1933. These mosquitoes were caught in barns; they are not found in houses during the winter. Among 609 *A. maculipennis* 11, or 1.8 per cent., were infected, mostly with sporozoites, and among 208 *A. superpictus*, 2, or 0.9 per cent., were infected with oöcysts. Precipitin tests made with mosquitoes which contained blood showed that *A. maculipennis* fed on man even during the hibernating period, and the authors conclude that these infections "may not be unimportant in explaining the spring rise of malaria which is so characteristic of the disease in the area."

Doctors H. E. MELENEY and J. A. CRABTREE made a survey of the rural houses of Lake County, Tennessee, during 1931. Most of these houses had been screened between 1927 and 1930, but the financial depression made it impossible to complete the 15 per cent. remaining unscreened, or to do any repairs. The data collected indicate that "although a tremendous effort had been expended by the county health department, the degree of protection afforded to the people from mosquitoes, even if they used what protection they had, was far from complete. . . . To what degree the imperfectly screened houses acted as traps in which infected mosquitoes might incubate and infect others is impossible to state. . . . The conclusion is reached that the screening and mosquito-proofing in Lake County probably were responsible for the greater reduction in incidence of malaria . . . its incompleteness and its unsatisfactory maintenance by the people have steadily decreased its value."

Dr. H. C. CLARK gave a review of malaria research during the year 1932-1933. He drew attention to the wide range of flight of some anopheles. This called for larval control over a longer radius than was formerly thought necessary, and greatly increased the expense. More attention should be paid to the screening of houses, and the treatment of carriers. Dr. Dalferes P. CURRY read a most interesting paper on the periodic long-distance flights of *P. albimanus*, Wied. The great artificial Gatun Lake, 165 square miles in extent, was completed in 1913 as part of the lock-system of the Panama Canal. It developed a flora of water-hyacinth (*Piaropus crassipes* and *P. azurcus*) and floating water-lettuce (*Pistia stratiotes*). The hyacinth, an inconvenience to navigation, has been controlled by arsenic spraying; the *Pistia* has disappeared spontaneously. In recent years, two other aquatic plants have invaded the lake. These are *Utricularia mixta*, a bladderwort, and several species of *Chara*. (Certain species of *Chara*, such as *C. foetida*, have been said to be inimical to mosquito breeding, but recent investigations indicate that they favour the development of mosquitoes wherever they grow.) The level of the lake sinks at end of the dry season, and the tops of these weeds come to the surface where they form a tangled mat in which incredible numbers of *A. albimanus* and *A. albimanus* breed. *A. albimanus* breeds in the *Utricularia*, it is not androphilous. *A. albimanus* is in the exposed patches of

Chara. In the hot, still weather, just before the rains, the sanitated areas of the Canal Zone are visited annually by flights of *A. albimanus*, that have flown 12 miles or more from Gatun Lake. A sharp rise in the malaria rate follows the flight. Formerly the Canal Zone was depopulated of all inhabitants except government employees, and these were concentrated in a few towns and villages; but repopulation by agricultural settlers (mostly West Indian negroes) has been allowed recently, and it is probable that the anopheles rest and feed in the cabins of these settlers during their long flight, for many of them are already infected when they reach the towns. "The Canal Zone, contrary to widespread opinion, and despite the great effort and large sums spent upon it, has not achieved complete mastery of its malaria problem . . . the excellent screening of the houses of the employees . . . is still a vital element in the protection of the health of the community. . . . It is believed that future control of Gatun Lake levels within smaller ranges of fluctuation, by means of a new storage lake now being created in the upper Chagres River Valley, may, to some degree, lessen the appearance of vegetation at the surface of Gatun Lake and, consequently, the production of anopheles."

The remainder of the papers read before the National Malaria Committee dealt with the malaria control work which had been done during the year in the several southern states. These are noted by title only on p. 146-8. Although funds had been reduced in many instances, a considerable amount of drainage work was done in several of the states by unemployed men who were engaged on relief work.

W. F.

APPELBAUM (Emanuel) & GELFAND (Ben B.). **The Artificial Trans-
mission of Malaria among Intravenous Diacetylmorphine Addicts.
A Preliminary Note on the Use of Atabrine in Malaria.**—*Jl. Amer.
Med. Assoc.* 1934. May 19. Vol. 102. No 20. pp. 1664-
1670. With 2 figs. [24 refs.]

This paper contains some interesting observations on the eye changes in cases of severe malaria among addicts.

The authors report 10 cases of malaria among drug addicts admitted to the Bellevue Hospital, New York, during the last six months. In most cases there was evidence that the disease had been contracted by sharing the hypodermic syringe with some other addict. The drug in common use by addicts is diacetyl morphine (heroin). In all the cases except one, the patients were severely ill. They were very anaemic; in only one was the red blood count above 4,000,000. Three of the cases were quartan and seven were subtertian. Six of the latter were suffering from cerebral malaria, and five of them died; one of the three quartan patients also died—making six deaths in 10 cases. The eyes were carefully examined in all cases. "Raynaud in 1892 . . . emphasized that the most common pathologic finding is hyperaemia of the disks and that this change is in most instances responsible for the transitory amblyopia" in cases of severe malaria. The hyperaemia of the finer vessels gives the disks a rosy brilliant appearance; this was observed in four of the patients. Retinal haemorrhages were seen in three. The authors were favourably impressed by atabrine.

- BRADLEY (Jas. A.). **Intravenous Transmission of Malaria in Drug Addicts.**—*Jl. Trop. Med. & Hyg.* 1934. Aug. 15. Vol. 37. No. 16. pp. 241–244. [11 refs.]
- . **Transmission of Malaria in Drug Addicts by Intravenous Use of Narcotics.**—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 319–323.

During the eleven months October 31st 1932 to September 30th 1933, 50 cases of malaria in drug addicts were admitted to the Charity Hospital of Louisiana, New Orleans, and 10 of them died. Evidence was obtained which showed that the infection had been transmitted by the syringe used for intravenous inoculation of the drug. [See also this *Bulletin*, Vol. 27, p. 202; Vol. 31, pp. 164–5; 419; 689.] W. F.

- WILSON (D. Bagster) & WILSON (Margaret E.). **On the Significance of Splenic Enlargement in East Africa.**—*East African Med. Jl.* 1934. Aug. Vol. 11. No. 5. pp. 156–165. With 2 charts.

The spleen rate alone is not a sure index of the malariousness of a given locality. For example, control in Tanga is so complete that no anopheles can be found in the houses, yet, owing to the migratory population becoming infected in other towns, the spleen rate is quite high. The spleen rate follows the parasite rate, and both decline as immunity rises, but a given degree of enlargement does not always mean the same degree of immunity. At the time when, judging from the infestation rates, immunity appears to be highest, that is between the ages of 15 and 30, the spleen rate and the degree of spleen enlargement are at their lowest. Individuals at this age can travel about with a freedom from malaria which is not possessed by persons of other ages. W. F.

- HINGST (Hans E.). ***Plasmodium falciparum* Welch, 1897. Does Direct Division of the Parasite precede Schizogony?**—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 325–328. With 1 fig.

The author raises again the question of the possibility of multiplication of the rings of *Plasmodium falciparum* by binary fission. He thinks that the presence in a red cell of 2, 4 and 8 rings cannot be explained in any other way. It is suggested that at the 4 stage each parasite may then become a schizont giving rise to 8 merozoites or a total of 32 in the cell. Certain photographs of red cells containing two or more parasites and single parasites with two chromatin dots are reproduced in support of the theory. C. M. Wenyon.

- MÜHLENS (P.). **Ueber *Plasmodium ovale* (Stephens).** [*Plasmodium ovale* (Stephens).]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Sept. Vol. 38. No. 9. pp. 367–374. With 21 coloured figs. on 1 plate & 10 text figs. [15 refs.]

The paper describes 4 cases of infection with *Plasmodium ovale*. Three were from West Africa and one from Western South America. In all cases the fever was of the tertian type. The characters of the parasite are illustrated in a coloured plate. As regards the individuality of this parasite the author thinks the final answer has not yet been given, though he inclines to the view that it does represent a fourth species as maintained by obsol. 30, p. 194. C. M. W.

TONKING (H. D.). **A Case of *Plasmodium ovale* in an East African Native.**—*East African Med. Jl.* 1934. Aug. Vol. 11. No. 5. p. 166.

Describes the distinguishing features of the parasites in another East African case.

STEPHENS's case (1922) came from East Africa [see this *Bulletin*, Vol. 20, p. 296]. The case here described came from the neighbourhood of Nairobi. The points observed were:—Almost every young form showed plentiful Schüffner's dots; half-grown parasites looked like *P. malariae* except for these dots. In parasites with the nucleus divided into three or more pieces, a large number of the containing red cells were oval in shape, and one end of the cell was drawn out into fine points. The parasite at this stage of growth was smaller than *P. vivax* of the same age. The most striking differences from *P. malariae* and *P. vivax* were seen in the sporulating forms, each of which contained only eight merozoites and a central mass of pigment in a cell with a tremendous number of Schüffner's dots. W. F.

HOPKINS (H. O.). **A Defibrinated Blood-Film Concentration Method for the Diagnosis of Malaria.**—*Malayan Med. Jl.* 1933. Dec. Vol. 8. No. 4. pp. 275-276.

In order to obviate certain disadvantages of the usual thick-film for malarial diagnosis, notably the difficulty of distinguishing the species of parasite in many cases, the author has adopted a method which appears to occupy an intermediate position between the thick and thin film. The blood to be examined, 3 or 4 cc., is taken from a vein and rapidly defibrinated in a tube with glass beads. The liquid portion is then transferred to a centrifuge tube and centrifuged. The supernatant fluid is removed and films of medium thickness, "thick thin films," are made from the concentrated cells. The films are very thoroughly dried, preferably in the incubator. They are then stained with a mixture of 3 cc. of distilled water (pH 7.2) and 2 drops of Giemsa. After washing gently in distilled water of the same pH the films are dried and examined. C. M. Wenyon.

TRENSZ (F.). Sur un nouveau procédé d'intradermoréaction pour le diagnostic de l'infection paludéenne. [**An Intradermal Reaction for the Diagnosis of Malaria.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. pp. 1082-1084.

ROCCHI [this *Bulletin*, Vol. 28, p. 1021] injected haemozoin intradermally and found that it produced a wheal in patients free from malaria but not in those who were infected. The author confirmed this and found that solutions of Seichi's melanine, and of metharfer Bouty acted in the same way as haemozoin [Haemozoin and melanine are not identical. See SINTON, this *Bulletin*, Vol. 31, p. 706.] W. F.

JAMES (S. P.). **The Direct Effect of Atebrin on the Parasites of Benign Tertian and Quartan Malaria.** [Laboratory Meeting Demonstration.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. p. 3. With 6 figs. on 1 plate.

A plate illustrates the changes in the parasites following a single dose of 0.6 gram of atebrin. The parasites become aggregated into lumps

and eventually disappears; the cytoplasm becomes thin and ragged, and breaks up; the nuclear vacuole is distended; the chromatin becomes opened out and diffuse, till finally only a few lightly stained dots remain.

W. F.

McnABB (P. E.) & SCHWARTZ (S. C.). Atabrine in the Treatment of Malaria in the Philippine Islands.—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 309-317. [11 refs.]

Eleven cases of benign tertian and three of subtertian were treated with atabrine. One of the latter had haemoglobinuria before atabrine treatment was begun. Treatment was successful in every case. A 5-day course appeared to be as effective as a 7-day course; there were no toxic symptoms. "No known relapses have occurred in one case after 4 months and in the remaining cases after 7 to 10 months."

W. F.

TAREEV (E. M.), BOLOTINA (A.), GONTAEVA (A.), RASKIN (A.) & EPSTEIN (E.). Sur le traitement du paludisme par l'atébriane. [**On the Treatment of Malaria with Atebrine.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. pp. 114-126. [In Russian. French summary p. 126.]

Atebrin (German and Soviet brands) was tested in the hospital of the Tropical Institute, Moscow, on 152 cases of malaria (80 B.T., 54 M.T., 11 Q), and produced a good clinical effect in all of them, including the most grave cases. It had a marked parasitocidal action upon all stages except the gametocytes of M.T. The only after-effect of treatment with atabrine was a slight discolouration of the skin ("pseudo-jaundice"). The drug was administered over a course of 5 days in doses of 0.1 gram 3 times a day. In some cases the cycle was repeated at intervals of 2-3 weeks. In the case of M.T., 0.03 gram plasmodicide was given together with atabrine 5 times *per diem*.

C. A. Hoare.

CHOPRA (R. N.) & SEN (B.). Atebrin in Heavy Infection with *P. falciparum*.—*Indian Med. Gaz.* 1934. July. Vol. 69. No. 7. pp. 392-393.

An Indian patient aged 59 suffering from a severe malignant tertian infection was treated with 0.3 grams of atabrine daily. At the beginning of treatment there were 180,000 rings per cubic centimetre. After 4 tablets there were 28,240 rings per cubic centimetre. After 5 there were only 13,800, and after 7 there were none. [The patient came from a district where malignant tertian prevails and had probably suffered from attacks of malaria for years].

W. F.

MANSON (D.). Relapsing Malaria.—*Indian Med. Gaz.* 1934. June. Vol. 69. No. 6. pp. 314-316.

A case in which atabrine proved unsatisfactory.

A young European woman was given 0.3 gram of atabrine and 0.01 gram of plasmoquine daily for 5 days, from August 27 to September 1, as a prophylactic. Four days after the end of treatment she had a temperature and symptoms of malaria, but no parasites could be found. Similar attacks followed, but repeated examinations disclosed no parasites. Finally, on October 21, she had a temperature of 102°, subtertian parasites were found in her blood and she was at last subjected to anti-malarial treatment, with an injection of quinine and not Vol. 30, p. of atabrine with plasmoquine.

About a month later, there was a relapse which was treated with quinine. This was followed by another relapse a month later which was treated with atebirin and plasmoquine, but this time, a parasitic relapse occurred 5 days later. Subsequently, atebirin was given only when parasites appeared in the blood and it was stopped as soon as they disappeared; this method proved more satisfactory, and the patient had little more fever until she left for Europe a few weeks later. There was no question of reinfection in this case [but it is always difficult to be certain that the doses prescribed are the same as the doses taken.] W. F.

MASSIAS (C.). Note sur le traitement du paludisme. [**Quinacrine Treatment of Malaria.**].—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 421-424.

Quinacrine appears to destroy all parasites except crescents.

Quinacrine is chloro-2-diethylamino-pentylamino-5-méthoxy-7-acridine. It is canary-yellow in colour, with a bitter taste and a neutral reaction. The dose is 0.3 grams daily in three doses. A course lasts five days and may be repeated after an interval of 5 days. Details are given of 5 cases of benign tertian and 1 case of subtertian treated with this drug. All forms of benign tertian parasites disappeared, and so did subtertian schizonts, but crescents persisted. No toxic symptoms were noted. W. F.

RAGIOT (Ch.) & ROBIN (L. A.). Essais de traitement du paludisme par la quinacrine. [**Treatment by Quinacrine.**].—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Mar. Vol. 12. No. 3. pp. 310-329. With 3 folding charts.

— & —. Essais sur le traitement du paludisme.—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 426-431.

This drug appears to resemble atebirin in its action.*

The authors treated one case of benign tertian, one case of quartan, and eight cases of subtertian. The patients were given three doses daily for 5 days, and each dose consisted of 0.1 gram. Clinical symptoms disappeared in 4 or 5 days and the schizonts within 5. Crescents were unaffected. There were no toxic symptoms. [See MASSIAS, above.] W. F.

RIOU (M.), GOURRY (N.) & HUSSENET (S.). Le paludisme en milieu indigène à Dakar pendant les années 1932-1933. Action comparée de divers médicaments. [**Malaria in Natives at Dakar, 1932-33. Action of Drugs compared.**].—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 579-586.

The results of quinacrine treatment are very good (see MASSIAS, above).

Among 1,199 patients there were 571 cases of subtertian, 548 of benign tertian, and 80 of quartan. Severe cases and large infections occur only in children. The authors have never seen a pernicious case in an adult native. Eighty cases treated with quinine and 70 treated with quinacrine were observed with special care. In 44 benign tertian cases treated with quinacrine, all the parasites had disappeared by the

*According to the Société Parisienne d'Expansion Chimique, the marketers of the Rhône-Poulenc anti-malarial, quinacrine is to be considered as 4 years of composition with atebirin. [Ed.]

third day. In subtertian and quartan cases the results of quinacrine treatment were as good as those with quinine. There were no true toxic symptoms but two patients complained of slight epigastric pain.

W. F.

SICAULT (G.). Note sur le traitement de dix cas de paludisme par un sel d'acridine. [**Treatment of Ten Cases of Malaria by an Acridine Salt.**—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 544-546.]

The successful intramuscular inoculation of quinacrine.

Three cases of benign tertian, three of subtertian, two of quartan, and two of mixed infection were treated with intramuscular injections of quinacrine dissolved in distilled water, in the proportion 0.1 gram in 5 cc. The doses given were from 0.005 to 0.01 gram per kilo of body weight, and one dose was given daily for 5 days. The patients were children between 3 and 9 years of age. The inoculations were not painful and the resultant swelling disappeared within 24 hours. The results were excellent; all parasites disappeared except crescents.

W. F.

MASSIAS (C.). Nouvelles observations de 48 paludéens traités par un dérivé quinoléique associé au quiniostovarsol. [**Treatment by a Quinoline Derivative with Quiniostovarsol.**—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 641-644.]

—. Dérivé quinoléinique employé seul contre le paludisme à *Pl. vivax* et à *Pl. praecox*.—*Ibid.* pp. 644-647.

Treatment by 574 F. alone and with stovarsol.

Doses of 0.02 gm. of 574 and 0.25 gm. of quiniostovarsol were given twice a day to 31 cases of benign tertian and 16 cases of subtertian with very good results. *P. falciparum* appeared to be more resistant than *P. vivax*. Quiniostovarsol favours the tolerance of 574, doses twice as large can be given with quiniostovarsol as without it.

Twenty-two cases of benign tertian and 4 cases of subtertian were treated with 574 alone. Several of the patients relapsed early, and there were 2 cases of intolerance with epigastric pains, anorexia, giddiness, etc. [See MASSIAS, this *Bulletin*, Vol. 31, p. 430, also SICAULT and DECOURT, *ibid.*, p. 431.]

W. F.

CHOPRA (R. N.), SEN (B.) & GANGULY (S. K.). **Malarcan in the Treatment of Indian Strains of Malaria.**—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 421-424.

"Malarcan is said to be a compound of a stereo-isomeric base of methyl-cupreine combined with methyl-acridinium-chloride and hydrocholic acid. It is probably a derivative of quinine or quinidine." The authors were supplied with this drug through the courtesy of Dr. P. REZAK of Vienna, and they employed it in the treatment of 29 cases of malaria. They found that it acted in the same way as quinine, both in the cure of the attack and in the extent to which it prevented relapses. They concluded that: "the drug is about 4 to 5 times more expensive than quinine and appears to have no advantage over that drug." [See this *BULLETIN*, Vol. 30, p. 202.]

W. F.

JOUKOV (N.), KRASSIKOVA (V.) & RYLOVNIKOVA (T.). Sur la méthode de traitement prophylactique des porteurs de gamètes par le plasmocide "A" et "B." [On a Method of Sterilization of Gamete-Carriers with Plasmocide.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. pp. 135-138. [In Russian. French summary p. 138.]

In a previous paper two of the present authors tested the prophylactic action of plasmocide A [this *Bulletin*, Vol. 31, pp. 174 & 178]. The present work records the results of tests on the prophylactic action of plasmocide B and upon the duration of the sterilizing effect of preparations A and B upon the gametocytes of the three species of malarial parasites, as manifested by their infectivity for *A. maculipennis* after treatment during one day with 6 doses of 0.015 gram of plasmocide A and of 0.03 gram of B respectively; the methods used were the same as in the preceding work.

Plasmocide B proved to have the same effect upon the gametocytes of B.T. and M.T. as plasmocide A, in that it lowered the rate of infection of the mosquitoes. Both preparations administered in doses referred to above prevented infection of the mosquitoes during 48 hours. Hence, in order to have a prophylactic effect, plasmocide should be given to gamete-carriers every third day. C. A. Hoare.

FIELD (J. W.). Notes on "Totaquina."—*Malayan Med. Jl.* 1934. June. Vol. 9. No. 2. pp. 26-30.

Therapeutically there is little to choose between totaquina and quinine. The only advantage of totaquina is its cheapness.

It will be remembered that totaquina is a form of cinchona febrifuge standardized to contain 70 per cent. of crystallizable alkaloids of which at least 15 per cent. must be quinine. Type I is prepared from the total alkaloids of *Cinchona succirubra*, Type II is prepared from *C. ledgeriana* residues with the addition of sufficient quinine to bring it up to specification. The author treated 417 patients with totaquina Type II, and a control series of 181 patients with quinine. The totaquina was obtained from Messrs. Howards of London. The patients were treated in the District Hospital adjoining the laboratory; thick blood film examinations and parasite counts were made daily during the period of treatment which lasted for 7 days. The drugs were given on a body-weight basis at the rate of 1 or 2 grams per 100 lbs. Tables 3 and 4 contrast the efficiency of totaquina with that of quinine in freeing the peripheral blood from parasites.

Rate of Disappearance of Non-Sexual Parasites from the Peripheral Blood after Commence- ment of Treatment.			S.T. Malaria 222 cases.
Within 1 day	Totaquina 9 per cent.	Quinine 12 per cent.	
" 2 days	27 "	40 "	
" 3 "	33 "	33 "	
" 4 "	14 "	9 "	
" 5 "	9 "	3 "	
" 6 "	5 "	2 "	
" 7 "	2 "	1 "	

Rate of Disappearance of Non-Sexual Parasites from the Peripheral Blood after Commencement of Treatment.		B.T. Malaria 78 Cases.	
Within		Totaquina 7 per cent.	Quinine 9 per cent.
1 day			
"	2 days	36	43
"	3 "	31	36
"	4 "	15	9
"	5 "	11	3
"	6 "	0	0
"	7 "	0	0

These tables show that the parasites disappeared rather more quickly with quinine than with totaquina. There was no significant difference in the time of disappearance of fever in the totaquina and quinine treated cases, nor was there any difference in respect of vomiting and toxic symptoms. When administered intravenously to rabbits in a 1 per cent. solution, no difference in the toxic effects of totaquina and quinine was evident. A dose of 2 grams per 100 lbs. body-weight was sometimes too much and a dose of 1 gram was sometimes too little. The author recommends something between the two; say 20 grains a day for the average Asiatic. It is most conveniently administered in capsules, or in powder form, washed down with water. It is not completely soluble in an acid mixture. It possesses no advantage over quinine except its lower price; at present totaquina Type II costs 1s. 4½d. an ounce as compared with quinine sulphate at 1s. 11d. An increased demand may send up the price of the residues from which it is manufactured. Large scale production of Type I would necessitate extensive planting of *C. succirubra*. Planters will not undertake this in the face of the growing popularity of the new synthetic remedies. The cinchona industry is threatened by these new drugs: the separation and purification of quinine is an expensive process; the total alkaloids can be extracted relatively simply and cheaply, and if the continued economic production of quinine on a large scale is seriously threatened, its replacement by a cheap cinchona product seems to be a possible development.

W. F.

SCHWETZ (J.) & BAUMANN (H.). Sur l'efficacité thérapeutique resp. prophylactique du cinchona fébrifuge, comparativement à celle de la quinine. [*Cinchona Febrifuge and Quinine Compared.*]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 3. pp. 353–364.

The authors used a febrifuge supplied by the Société Produits Roche. It contained 60 per cent. of active alkaloids as compared with 73 per cent. in the quinine sulphate which is usually employed. But while its alkaloidal content was only 20 per cent. less than that of quinine, its price was half; quinine costs 1s. 8d. and cinchona febrifuge costs 10d. an ounce. The author found that when the febrifuge was given in the same doses as quinine, the results were almost the same, but when the dose of febrifuge was twice as large, the results were better. W. F.

COLLINS (Ralph K.). **A Field Experiment in Quinine Treatment.**—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 329–338.

The treatment of malaria with short courses of quinine lasting 4 days is recommended.

This paper concerns observations made at the Petrich (Bulgaria) Station for Field Studies in Malaria. The prolonged method of treatment advised for general use by the National Inspectorate of Malaria in Bulgaria, consists of 1 gram of quinine daily for 8 days, repeated after an interval of 5 days, and then succeeded by a period of prophylactic treatment which lasts altogether for 77 days and consumes 32 grams of quinine. The short method of treatment used by the author consisted of 1 gram of quinine sulphate daily for 3 or 4 days on the occasion of each acute attack, and he states that "the striking feature of our experience is the fact that the majority of the patients suffered but a single acute attack during the malaria season. . . . The number of 'well' days without treatment experienced by persons receiving minimal doses for their acute attacks is considerably greater than in the case of patients receiving a prolonged course of treatment. At the same time the danger of recrudescence is only slightly greater." There is also a saving of about £7 on every 100 cases treated by the shorter method.

W. F.

SMITH (E. C. Temple). **Quinine Amblyopia.**—*Med. Jl. Australia.* 1934. Sept. 1. 21st Year. Vol. 2. No. 9. p. 289. With 1 chart.

Amblyopia after 15 grains of quinine; but the evidence is untrustworthy.

The author was called to see a young unmarried woman who had become suddenly blind. She first denied having taken any drug, and then said that she had taken 15 grains of quinine. (She had missed one monthly period.) The pupils were widely dilated and immobile. Three weeks later, the visual fields were much restricted, the discs were pale and the arteries contracted. No further history was obtainable.

W. F.

NAUCK (E. G.). Chemotherapeutische Versuche bei Affenmalaria (*Pl. knowlesi*). [**Chemotherapy in Monkey Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Aug. Vol. 38. No. 8. pp. 313–326. With 12 figs. [12 refs.]

Experiments carried out on monkeys infected with *P. knowlesi* to test the therapeutic value of certain antimalaria drugs.

The drugs employed were quinine, atebrin and plasmoquine. The effective dose is higher in the case of all three drugs than the dose for man. With sufficiently high doses of atebrin monkeys can be cured with certainty; not only do they remain free from relapses, but they can be infected with the homologous strain of malaria parasite shortly after cessation of the infection. Quinine and plasmoquine act more slowly on the dividing forms than atebrin. The special gametocidal property of plasmoquine could not be determined. Better results were obtained with quinine and plasmoquine in combination than with either alone. Atebrin cannot prevent relapses with certainty. Treatment with atebrin towards the end of the incubation period prevents the occurrence of infection. Atebrin tolerance (Festigkeit) was not observed.

E. D. W. Greig.

BOVET (D.), BENOIT (G.) & ALTMAN (R.). Action thérapeutique de quinoléines à poids moléculaire élevé, homologues de la plasmoquine, sur les hématozoaires des calfats et des serins. [Therapeutic Action of Quinolines of High Molecular Weight on Haematozoa of Calfats and Canaries.]—*Bull. Soc. Path. Exot.* 1934. Mar. 14. Vol. 27. No. 3. pp. 236–242. With 1 fig. [11 refs.]

The characteristic feature of the new anti-malarial drugs is the presence of a dialkylaminoalkylamino- side chain: $\text{HN}(\text{CH}_2)_n\text{NRR}'$. In plasmoquine and atebirin the chain is branched and $n=5$, $\text{HN}\cdot\text{CH}(\text{CH}_3)\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{N}(\text{C}_2\text{H}_5)_2$, and is attached to a methoxyquinoline and a chloromethoxyacridine nucleus respectively. The authors have examined the action of a series of homologues of plasmoquine with unbranched chains where $n=2$ to 11. The graph obtained by plotting minimal effective doses of the various compounds against values of n is roughly parabolic with summits at $n=3$ and $n=5$. This is for calfats (Java sparrows) parasitized with *Haemoproteus* and may be taken as a measure of activity against the sexual form of the parasite. When the same set of compounds is tested in avian malaria in canaries the activities for the higher values of n are almost as great as for the lower values of n in the calfat. Thus the chemotherapeutic index when $n=11$ is 1/100 for the canary and 1/3 for the calfat, and it is assumed that the higher activity in the canary must be due to action on both the sexual and asexual forms of the parasite. If this assumption is valid, it should be possible to synthesize drugs active against both forms, and it follows that increase of the molecular complexity, as in the replacement of quinoline by acridine in passing from plasmoquine to atebirin, or by lengthening the side chain in plasmoquine, causes a change from activity against sexual to activity against asexual forms.

T. A. Henry.

LOURIE (E. M.). Studies on Chemotherapy in Bird Malaria. 1.—Acquired Immunity in Relation to Quinine Treatment in *Plasmodium cathemerium* Infections.—*Ann. Trop. Med. & Parasit.* 1934. July 12. Vol. 28. No. 2. pp. 151–169. With 1 fig.

Early treatment with large doses of quinine does not interfere with the development of immunity. An interesting and important paper.

The ordinary course of infection in a canary, after intramuscular or intraperitoneal inoculation with *Plasmodium cathemerium*, is as follows: An incubation, or prepatent period, of 2 to 4 days is followed by the appearance of parasites in the blood which increase rapidly for about 4 days; then a crisis occurs which involves a striking disappearance of parasites from the circulation. A few may be found for a week or two longer, and then the bird passes into the latent stage during which, while no parasites can be found, inoculation of its blood into another bird will produce an infection. During this latent stage, the bird is immune to superinfection. The first object of the author's work was to determine whether this immunity was as effective in birds which had been treated with quinine from the earliest stage of infection, as it was in birds which had not been treated at all. With this in view, a series of birds was treated with injections of quinine which were begun a few days after the inoculation of the *P. cathemerium* infection and were continued for a fortnight. About 6 weeks later, these birds and

a control series which had not been treated with quinine were reinoculated with *P. cathemerium*. The result showed that the early treatment had not interfered with the production of immunity. When the acute phase was suppressed by quinine there developed as powerful an immunity to superinfection as is acquired when an infection is not subjected to any treatment.

It was also found that when very large numbers of parasites were inoculated into canaries during the latent stage, they disappeared at least as quickly in the birds which had been previously treated with quinine as in those which had received none. If the early prophylactic quinine treatment was continued for more than 10 days, the number of parasites appearing in the blood after its termination was always less than the number in untreated birds. This indicates that "the immunity enjoyed by birds which have been subjected to such treatment is largely built up during the actual course of its administration . . . most of the birds treated for longer periods than 3 weeks were frankly carried right over into the latent stage of infection." These points are of importance not only theoretically, but also as regards certain problems of human malaria. "These findings do not correspond with the theory that in human malaria the early exhibition of quinine must interfere significantly with the acquirement of immunity or tolerance," but "the finding of a set of circumstances in one form of malaria does not necessarily establish a general rule for all malarias." Daily injections of quinine, up to a quarter of the minimum lethal dose, did not result in sterilization of *P. cathemerium* infections. W. F.

ROSKIN (Gr.) & ROMANOWA (K.). Arzneistoffe und Ultraviolettstrahlen. XIII. Mitteilung. Kombinierte Therapie bei Vogel-malaria. [Combined Therapy with Drugs and Ultraviolet Rays in Bird Malaria.]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. July 23. Vol. 82. No. 5/6. pp. 461-474.

Experimental research to determine the effect of ultra-violet rays in augmenting the action of salvarsan preparations in the treatment of bird malaria.

The authors conclude that novarsolan exerts a certain therapeutic effect in light infections of bird malaria. If non-therapeutic doses of novarsolan are given simultaneously with ultra-violet rays no effect is noted. From this it may be accepted that in canaries the "factor A" is either not produced or in very small quantities [see this *Bulletin*, Vol. 28, p. 912]. In mice on the contrary it is produced. The serum of irradiated mice increases the therapeutic properties of novarsolan and neosalvarsan in bird malaria. This indicates that "factor A" can activate neosalvarsan preparations in the organism of animals which belong to a different species to those in which it was produced. "Factor A" produced by radiation of mice possesses the character of an "activator." [*loc. cit.*, Vol. 29, p. 353.] E. D. W. Greig.

SHAH (K. S.). The Periodic Development of Sexual Forms of *Plasmodium cathemerium* in the Peripheral Circulation of Canaries.—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 392-403. With 6 figs. & 2 graphs. [14 refs.]

In canaries experimentally infected with *Plasmodium cathemerium* the time of appearance of gametocytes, the number of these present and

their attainment of maturity is strictly parallel to the appearance, development and number of the asexual forms. Whenever asexual forms are present gametocytes are present also, while the reproduction of the schizonts at about 6 p.m. is associated with the arrival at maturity of gametocytes which at that stage of their development have completely displaced the nucleus of the host cell. The growth of the gametocyte from the merozoite takes place in the peripheral blood.

C. M. Wenyon.

HUFF (Clay G.) & GAMBRELL (Elizabeth). **Strains of *Plasmodium cathemerium* with and without Gametocytes.**—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 404–415. With 4 figs. [19 refs.]

Two strains of *Plasmodium cathemerium* after a number of bi-weekly passages from canary to canary became completely gametocyteless. Another strain after similar treatment still retained a few gametocytes while other strains continued to produce them in large numbers. Birds after recovery from an infection of a gametocyteless strain, which had lost its regular periodicity, had become slightly more virulent and was showing an altered staining reaction, were immune to infection with a normal strain, the normal parasites injected, both asexual and sexual forms, being quickly removed from the blood. These parasites, though removed from the blood, remained in the bird's system as a latent infection for at least eight months along with the atypical strain.

C. M. W.

BOYD (Geo. H.) & ALLEN (Lane H.). **Adult Size in Relation to Reproduction of the Avian Malaria Parasite, *Plasmodium cathemerium*.**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 73–83. With 4 figs. [11 refs.]

A study of *Plasmodium cathemerium* in canaries has shown that the average size of the parasites is usually greatest at the commencement of an infection and decreases as the parasites become more numerous, only to increase again as the attack subsides. The variation may be as much as 39 per cent. of the maximum size. In spite of this the reproduction periods occur regularly at about 6 p.m. each day, the number of merozoites produced being directly dependent on the size of the schizont. It thus appears that the initiation of schizogony is not determined by the size of the parasite. The rate of growth of the parasite could be retarded by the administration each day of four doses of one-fourth of a mgm. of quinine hydrochloride.

C. M. W.

MANWELL (Reginald D.). **The Duration of Malarial Infection in Birds.**—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 532–538. [20 refs.]

By observations on 118 birds which had recovered from infections with one or other of five species of malarial parasite it was shown that parasites persisted in the body throughout the period of observation which was not less than a year in any case and three years in a few instances. The results show that great caution must be exercised before concluding that an infection in a bird has been completely removed even when inoculation of blood into a clean bird fails to produce infection.

C. M. W.

FINDLAY (G. M.) & BROWN (H. C.). **The Relation of the Electric Charge of the Red Cells to Phagocytosis in Avian Malaria.**—*Brit. Jl. Experim. Path.* 1934. June. Vol. 15. No. 3. pp. 148–153. With 2 figs. [11 refs.]

One of the authors (H.C.B.) has already shown that the serum from a canary with a latent malarial infection is capable of reducing the electric charge not only of canary red blood corpuscles but also of mouse corpuscles and even bacteria, and that this property is related to an increase of the euglobulin fraction of the serum leading to the formation of a layer of euglobulin on the surface of the antigen. In the present paper evidence is produced which suggests that the serum of canaries with latent malaria is capable of sensitizing infected red cells in rendering them more susceptible to phagocytosis, as evidenced by an increase in the incubation period after inoculation of the sensitized cells into clean birds. It is further noted that blood from a canary recovering from a malarial attack produces infection less readily than blood taken at the beginning of the attack, even when the number of infected cells injected is approximately the same. The electric charge of the cells during an attack is correlated with the size of the spleen and the degree of phagocytosis of infected cells by the macrophages in this organ.

C. M. W.

SERGEANT (Etienne). **Météorologie et rechutes de paludisme (phases lunaires, pression barométrique).** [**Meteorology and Malarial Relapses.**]—*Arch. Inst. Pasteur d'Algérie.* 1934. June. Vol. 12. No. 2. pp. 201–204. With 2 graphs.

This paper deals with relapses during the latent stage in canaries infected with *Plasmodium relictum*; 212 relapses have been observed in 116 canaries at the Pasteur Institute of Algiers during 22 years. It was found that these relapses occurred most frequently during the period between the first quarter of the moon and the full moon. HUCHON has noted that the same occurs in human malaria. The author also found that the greatest number of relapses occurred when the maximum barometric pressure was low.

W. F.

SERGEANT (Edm.), SERGEANT (Et.) & CATANEI (A.). **Un type de maladie à prémunition: le paludisme des passereaux à *Plasmodium relictum*.** [**Passerine Malaria (*P. relictum*), a Type of Premunition Disease.**]—*Ann. Inst. Pasteur.* 1934. Aug. Vol. 53. No. 2. pp. 101–119. With 5 figs. [Refs. in footnotes.]

In this article the authors discuss the whole question of immunity in bird malaria, which they regard as a definite premunition. A canary inoculated with one species of bird malarial parasite has an acute attack from which it may recover. If it does so the infection becomes a chronic one in which a balance is struck between the host and the parasite. The parasites in the bird are so few in number that their presence can only be detected by the inoculation of large quantities of blood into susceptible birds. The chronic infection in the canary has been found to persist for from 1 to 5 years during which period the bird cannot be reinfected with the same strain of parasite. Directly the bird loses its infection completely there is no longer any immunity, the bird being as susceptible to inoculation as it was originally. The

authors have never observed a case of a canary naturally resistant to a first infection, while they have found that the serum taken from a bird during its premunition stage cannot confer immunity on another bird. It is not possible to produce an immunity by the inoculation of killed parasites, for birds are never immune unless parasites are present in the body. The only type of vaccination obtainable is one in which the initial acute attack is avoided, the bird after inoculation passing directly into the condition of premunition. This occurs naturally in the case of some birds, but can be brought about by the use of certain drugs which are capable of preventing the acute attack or by the inoculation of altered parasites, such as old sporozoites from the salivary glands of mosquitoes or those parasites which occur in the blood of a bird soon after inoculation and before parasites are actually detectable by microscopic examination in its blood, in other words, by the inoculation of blood taken from another bird during the period of incubation.

C. M. Wenyon.

ROUBAUD (Emile) & MEZGER (Jean). Sur la sensibilité au paludisme des oiseaux (*Plasmodium relictum*) des divers peuplements raciaux du moustique commun, *Culex pipiens* L. [**Susceptibility to Bird Malaria of Various Races of *C. pipiens*.**—*C. R. Acad. Sci.* 1934. July 9. Vol. 199. No. 2. pp. 170-172.]

HUFF has shown that if a number of *Culex pipiens* taken at random are fed on birds with malaria the infection of the mosquitoes is not uniform, some even failing to become infected. He has also shown that the descendants of such resistant individuals are also resistant, so that by selection it is possible to establish resistant strains of this mosquito. [See this *Bulletin*, Vol. 27, p. 892.] The authors of the paper under review have tested the susceptibility to bird malaria infection of three natural races of *Culex pipiens*. Two of these, *C. pipiens pipiens* and *C. pipiens berbericus* are open air, rural or garden races which normally have access to birds, the former in France and the latter in N. Africa, while the third is an autogenous race of *C. pipiens* which has adapted itself to urban surroundings where it feeds on man rather than on birds. The result has been that whereas the last named race always becomes infected so that 100 per cent. of the exposed mosquitoes show over 10 oöcysts, the two rural races become infected very irregularly, the first giving 32 per cent. and the second 48 per cent. of individuals which either resist infection entirely or show less than 6 oöcysts. This result seems to suggest that, like human beings, mosquitoes which have been constantly exposed to bird malaria infection acquire a certain immunity which is entirely absent in the race which rarely, if ever, feeds on birds.

C. M. W.

RAFFAELE (Giulio). Sul comportamento degli sporozoi nel sangue dell'ospite. [**The Behaviour of Sporozoites in the Blood of the Host.**—*Riv. di Malarologia.* 1934. Vol. 13. No. 4. pp. 395-403. English summary (9 lines).]

The author carried out many experiments—nine groups *in vitro* and three *in vivo*—using the sporozoites of the avian parasite *P. praecox*, obtained from the salivary glands of *Culex* and also mature oöcysts, with a view of ascertaining the penetration of sporozoites into the red corpuscles. He placed them in contact with blood itself (of a goldfinch), with serum first, then blood, with normal saline and blood, at

different temperatures and for varying lengths of time. In the *in vivo* experiments he injected the glandular contents into the thigh muscles, or subcutaneously, or directly into the blood stream. The results in each case were negative and the author concludes that "sporozoites inoculated by mosquitoes do not provoke the infection through immediate penetration in the circulating erythrocytes; on the contrary, they seem to be rapidly destroyed." H. H. S.

GIOVANNOLA (Arnaldo). Tentativo di classificazione dei plasmodi aviari. [Classification of the Avian Plasmodia].—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 3. pp. 372-379. With 24 figs. on 1 plate. English summary.

The number of known species of malarial parasites of birds has increased considerably in recent years. Apart from the originally described *Plasmodium praecox* (or *P. relictum*, as some maintain it should be), a comparatively large parasite with spherical schizonts and gametocytes producing considerable deformity of the host cell, other species have been discovered which are either much smaller in size than *P. praecox* and produce a correspondingly smaller number of merozoites, or possess elongate gametocytes which, surrounding the nucleus, often render differentiation from halteridium a matter of difficulty.

The author of the paper under review tabulates the known species under three headings—1, forms which have spherical gametocytes and cause displacement of the nucleus of the host cell; 2, forms which have elongate gametocytes and displace the nucleus; 3, forms with elongate gametocytes and no nuclear displacement. To the first group belong *P. praecox*, *P. cathemerium*, *P. capistrani* and *P. wasielewski*; to the second *P. elongatum*; to the third *P. rouxi*, *P. tenue*, *P. circumflexum* and *P. fallax*. The paper gives the differential diagnosis of these species and a plate illustrating the various types. C. M. W.

SINTON (J. A.) & MULLIGAN (H. W.). Mixed Infections in the Malaria of the Lower Monkeys. Part I. Mixed Infections as the Cause of Apparent Variations in the Morphology and Pathogenicity of Simian Plasmodia. Part II. The Probable Occurrence of Mixed Infections in Some of the Older Records of Monkey Malaria.—*Records of the Malaria Survey of India*. 1933. Dec. Vol. 3. No. 4. pp. 719-767. [38 refs.]; pp. 769-808. [73 refs.]

In a paper published in 1932 (this *Bulletin* Vol. 29, p. 701) KNOWLES and Das GUPTA reported the discovery in what they took to be an African monkey, *Cercopithecus pygerythrus*, of a scanty plasmodium infection which they successfully inoculated to other monkeys and also to man. It was noted that in *Silenus rhesus* the infection was severe and fatal while in *C. pygerythrus* it was mild. Furthermore the morphology of the parasite was different in the two hosts and it was concluded that this variation was due to differences in the influence on the parasite of the two hosts. It was later pointed out by KNOWLES (Editorial, *Indian Med. Gaz.*, Vol. 67, p. 701) that the original monkey and the others with which he and Das GUPTA had worked under the name of *Cercopithecus pygerythrus* was actually *Silenus irus* (*Macacus cynomolgus*), an oriental species. The new principle which was introduced into parasitology by the assumption that the host was able to influence so profoundly the morphology of a parasite seemed to the

authors of the paper under review so important that they felt it advisable to investigate the matter further with a view to finding out if some other explanation might not account for it.

In Part I of this paper they describe in detail a long series of careful experiments and observations all of which lead to one conclusion, namely that the original monkey found infected by KNOWLES and Das GUPTA and others of the same species investigated later were actually harbouring two distinct parasites, one of which was *Plasmodium inui* var. *cynomolgi* Mayer, 1907 and the other *P. knowlesi* Sinton and Mulligan, 1932. Pure strains of these two forms were obtained by methods which are described. It is noted that each retained its morphological characters, whether infecting *S. rhesus*, *S. irus* or *S. sinicus* and that there was no indication whatever that a series of passages in one species or a transfer to another one was able to bring about any change in morphology. It is shown that *P. knowlesi* is particularly virulent for *S. rhesus*, so that when a monkey of this species is inoculated with a mixed infection, either the naturally occurring one or one intentionally produced, it is *P. knowlesi* which is most evident. On the other hand in mixed infections in *S. irus*, which are mild in nature, it is *P. inui* var. *cynomolgi* which is most prominent. Passaged to a monkey of a different genus, *Pygathrix schistaceus*, *P. knowlesi* again retained its characteristic morphology. Amongst other differences between the two parasites it is noted that the schizogony cycle of *P. knowlesi* is 24 hours while that of *P. inui* var. *cynomolgi* is 48 hours. Attempts to transmit *P. knowlesi* by mosquitoes failed, though on several occasions development up to the occurrence of sporozoites in the salivary glands of *Anopheles annularis* (*A. fuliginosus*) was obtained. With *P. inui* var. *cynomolgi*, on the other hand, healthy *S. rhesus* were infected on three occasions by the bites of *A. annularis* and once by *A. subpictus*, while oöcysts and salivary gland infection with sporozoites were found in a high percentage of these mosquitoes as well as *A. maculatus*, *A. culicifacies* and *A. splendidus* fed on infected animals. It was noted that in attempts to produce infection by injection of sporozoites from ruptured oöcysts or from freshly infected salivary glands failure always resulted. It is suggested that some period of maturation of sporozoites in the salivary glands may be necessary before they become infective. In work of the kind discussed in this paper it is evidently of the utmost importance that the monkeys used for inoculation purposes be free from latent infection. The methods of detecting such latent infections with a view to the exclusion from experiments of already infected animals are described, as also those employed for isolating pure strains of one or other species of malarial parasite from mixed infections such as occur very commonly in *S. irus*. The monkey *S. rhesus*, so largely employed for the experiments, has never been found by the authors to have a natural malarial infection though they have submitted it to the most careful tests.

In the second part of the paper the authors discuss the general question of mixed infections of malarial parasites in monkeys. A number of observers have recorded changes in morphology of parasites, the staining reactions of the host cells and the pathogenicity in passages from one species of monkey to another. The work conducted with *P. knowlesi* and *P. inui* var. *cynomolgi* has shown that all these so-called changes may be caused by unrecognized mixed infections, so that many of the older descriptions and accounts of malarial parasites of monkeys are correspondingly inaccurate. From this point of view the authors

examine the literature of the subject and come to the general conclusion that unrecognized mixed infections are responsible for many confusing statements and discrepancies. It is evident that the specific morphology of these parasites will require reinvestigation in the light of the experiences gained by the studies described in this paper. With a view to assisting in the re-examination there is given a list of the genera of African and Asiatic monkeys in which malarial parasites have been found and in which some indication of the degree of prevalence has been noted.

The above account of this valuable paper does little more than give an outline of its contents. It is full of the most useful detail which will be invaluable to all who contemplate investigations on monkey malaria. The authors have found themselves in a very favourable position for such an investigation, with an abundance of material in the shape of naturally uninfected animals like *S. rhesus*, so that it may be said that for the first time there has been conducted a thorough investigation of a single malarial parasite of monkeys. The thoroughness of this work and the results obtained rather suggest that many of the previous accounts of malarial parasites of monkeys have little other value than the mere record of a malarial infection in a particular monkey.

C. M. W.

MALAMOS (B.). Das Blutbild bei Affenmalaria. [**Blood Picture in Monkey Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Sept. Vol. 38. No. 9. pp. 374-386. With 8 figs. [11 refs.]

Observations on the blood changes in monkeys following the inoculation of *Plasmodium knowlesi*.

In the investigations the monkeys chiefly employed were *Mac. cynomolgus* (syn. *S. irus*), also one *Mac. rhesus* (syn. *M. mulatta*) and one *Cercopithecus mona*. The strain of *Plasmodium knowlesi* used was obtained from London.

Blood counts of normal monkeys give :—*Cercopithecus* 19,600 leucocytes, 5,950,000 erythrocytes and 58 per cent. haemoglobin, *Mac. rhesus* 16,000 leucocytes, 5,200,000 erythrocytes, and 60 per cent. haemoglobin. The author was struck by the low haemoglobin value compared with high count of the red cells ; the colour index is low, 0.6.

As a result of his experimental study the author concludes that *Plasmodium knowlesi* infection in the monkeys employed causes a severe toxic anaemia by destruction of the red cells and blocking of the blood forming organs. The peak of the anaemia occurs towards the end of the infection and it may reach a high degree, the red cells and haemoglobin dropping to 1,000,000 and 21 per cent. respectively. The character of the anaemia is micro-macrocytic with aniso- and poikilo-cytosis, polychromatophilia and Cabot's rings. Spontaneous regeneration occurs very rapidly with many normoblasts and macroblasts. Shortly after the infection a leucocytosis occurs, the white cells rising to 26,400, soon followed by a leucopenia, the leucocytes falling to between 12,000 and 15,000, in one case 4,000, the latter chiefly due to a diminution of polynuclears ; a shift to the left does not occur. During regeneration myelocytic cells are numerous owing to stimulation of the bone marrow. Resistance to the infection is accompanied by a high grade monocytosis ; many of these cells are laden with parasites and pigment. During the infection the number of lymphocytes is not diminished, but rather slightly increased. In fatal

infections in splenectomized animals the number of monocytes and lymphocytes is much diminished compared with infected non-splenectomized monkeys.

E. D. W. Greig.

MALAMOS (B.). Die Rolle des Retikulo-Endothelialen Systems, insbesondere der Milz bei Affenmalaria. [**Rôle of the Reticulo-Endothelial System, particularly the Spleen in Monkey Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Aug. Vol. 38. No. 8. pp. 326–342. With 7 figs. [20 refs.]

An experimental study of the part played by the reticulo-endothelial system and particularly the spleen in monkeys infected with *Plasmodium knowlesi*.

Normally infection with *Plasmodium knowlesi* in *Macacus cynomolgus* runs a chronic course and requires no treatment, but if the spleen is removed or the R.E.S. is blocked with trypanblue or Indian ink the animals die in from 4–9 days after appearance of parasites if not treated. It does not matter at what stage splenectomy is performed, whether a long time before or in the chronic phase of infection; whereas a blockade can only raise the virulence when administered before infection and has no effect whatever in the chronic stage. The treatment of splenectomized and blockaded monkeys with atebirin, quinine, and quinine and plasmoquine gave exactly the same results as in non-splenectomized monkeys, so the spleen is not necessary for this form of therapy.

E. D. W. Greig.

MALAMOS (B.). 'Ueber eigentümliche Parasitenkapseln bei menschlicher Malaria (*Pl. vivax* und *Pl. ovale*) und Affenmalaria (*Pl. knowlesi*). Vorläufige Mitteilung. [**Peculiar Parasite Capsule in Human and Monkey Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Aug. Vol. 38. No. 8. pp. 342–349. With 14 figs. on 1 plate. [18 refs.]

A peculiar capsule formation is described in connexion with the *Plasmodium vivax* and *ovale* in man, and the *P. knowlesi* in monkeys.

A definite capsule which stains like chromatin with Giemsa is seen round the parasites. It cannot be definitely stated whether the capsule forms part of the parasite or the red cell containing it. It is only seen in schizonts, and chiefly in the early dividing forms. A curious morphological alteration occurred in splenectomized superinfected monkeys: the capsule was seen to break up into loops or to become entirely dissolved. During the division of the parasites a body was observed inconstantly, which was not pigment, but clumps of blue staining protoplasm that often contained pigment.

E. D. W. Greig.

SCHWETZ (J.). Recherches sur la malaria congénitale et l'infection malarienne du placenta dans la malaria endémique de l'Afrique Centrale. Deuxième étude. [**Congenital Malaria and Malarial Infection of the Placenta in Central Africa.**]—*Riv. di Malariologia.* 1934. Vol. 13. No. 4. pp. 435–442. With 17 coloured figs. on 1 plate.

Adult schizonts were found in the placenta; young rings and crescents were found in the peripheral blood. No congenital malaria was found [but see SCHWETZ & PEEL, below].

No malaria was found in 33 newly born native infants although parasites were present in 21 of the mothers. Parasites were far more numerous in the placenta than in the peripheral blood of the mothers. The young rings and crescents which are commonly found in the peripheral blood are rare in the placenta. Here adult schizonts of *P. falciparum*, pigmented or in division, are the commonest forms. *P. malariae* was found in the peripheral blood of three mothers, and *P. vivax* in the blood of one, but these species were not found in the placenta. Possibly, the tropism of *P. falciparum* for the internal organs is the reason for the persistence of this species in the adult native. [See this *Bulletin*, Vol. 23, p. 130 (BLACKLOCK & GORDON).]

W. F.

SCHWETZ (J.) & PEEL. **Congenital Malaria and Placental Infections amongst the Negroes of Central Africa.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 167–174.

The placenta behaves as a true internal organ and contains adult dividing forms of *P. falciparum*. Out of 56 cases, the infant was congenitally infected in two (see also SCHWETZ above).

The authors examined 56 native women at the time of childbirth with the following results:—

(a) Peripheral blood of mother.	Percentage infected	...	68.0
(b) Placental blood	"	"	74.0
(c) Cord blood	"	"	6.0
(d) Infant's blood	"	"	3.6

The parasites seen in the blood taken from the mothers, the infants, and the cords were young schizonts. In the placentas numerous fully grown forms were seen (pigmented and in division), and some were undergoing phagocytosis. The placenta behaved as a true internal organ, like the spleen, in containing the adult schizonts of *P. falciparum*. In 16 per cent. of cases, a heavy placental infection was found although there were no parasites in the peripheral blood. In no case did the placental infection appear to have a detrimental influence on the child. "Though congenital malarial infection is possible even in children born of mothers who are healthy though infected, in practice it is of little importance since the high parasite index of native children, and even of infants, is the result of infections acquired after birth." W. F.

DAVIS (Nelson C.). **The Microscopical Examination of 29,593 Human Livers from Central and Northern Brazil, with Special Reference to the Occurrence of Malaria and Schistosomiasis.**—*Amer. Jl. Hyg.* 1934. May. Vol. 19. No. 3. pp. 567–600. With 6 charts & 3 maps. [14 refs.]

This paper deals with the diagnosis of malaria, schistosomiasis and yellow fever by means of the examination of liver sections.

A large number of specimens of liver have been collected by means of an instrument specially designed for the rapid removal of liver tissue by laymen without autopsy [see this *Bulletin*, Vol. 31, p. 836]. By this means yellow fever was detected in 43 places where it was not known to be present. The present paper concerns the distribution of malaria and schistosomiasis as indicated by this method, and their diagnosis from yellow fever by means of the examination of the liver

tissue. Unequivocal histopathological diagnosis of intestinal schistosomiasis rests on finding eggs surrounded by an inflammatory reaction which produces characteristic nodules. In early stages, if eggs cannot be found, the appearances resemble those of other diseases which produce miliary granulomata. Pigmentation may resemble that of malaria, but the pigment is chiefly confined to the portal zone and is concentrated in the nodules. The pigment is usually fine and dust-like, whereas, in malaria, much of it is in the form of round, shot-like bodies. "Malaria, either alone or complicated by blackwater fever, is capable of producing lesions which may be confused with those of yellow fever." This is particularly the case in fulminant malaria and blackwater fever. In malaria the necrosis is typically central, while in yellow fever it is midzonal; but variations occur. *W. F.*

SINTON (J. A.) & GHOSH (B. N.). **Studies of Malarial Pigment (Haemozoin). Part III. Further Researches into the Action of Solvents, and the Results of Observations on the Action of Oxidising and Reducing Agents, on Optical Properties, and on Crystallisation.—Records of the Malaria Survey of India. 1934. June. Vol. 4. No. 2. pp. 205–221. With 2 charts. [17 refs.]**

Haemozoin and haematin are apparently identical. The authors conclude that :—

- (a) The rates of solution of haemozoin and haematin are the same.
- (b) Reducing agents produce the same effect on both the pigments.
- (c) Spectroscopic measurements suggest strongly that the two substances are identical.
- (d) Crystals of haematin chloride and haematin iodide can be formed from haemozoin, and the crystals are indistinguishable from those obtained from haematin.
- (e) Pyridine-haemochromogen crystals can be obtained both from haematin and from haemozoin.

"As a result of these and our previous experiments we consider that the pigment found in *P. knowlesi*, a malarial parasite of lower monkeys, is indistinguishable from haematin." *W. F.*

JAMES (S. P.). **The Shute Method of making Preparations of Ex-flagellating Gametocytes and Oökinetes of Malarial Parasites. [Correspondence].—Trans. Roy. Soc. Trop. Med. & Hyg. 1934. June 30. Vol. 28. No. 1. pp. 104–105.**

The method is thus described :—

"For ex-flagellation of male gametocytes.—Prepare four Petri dishes by fitting two layers of filter paper accurately cut to size in the top half of each dish, and the same in the bottom half. Moisten the filter paper with as much water as it will absorb, but not more. Lay a triangular piece of glass tubing in each dish and place the four dishes in a moist atmosphere incubator at 25°C. for two hours. The dishes should not be piled on one another. When the blood is to be examined, take the dishes (each wrapped in cloth so that it does not become cold) and prepared slides to the bed of the patient with an assistant who will hold a separate dish ready for each blood film as it is made. Prick the finger, make a thin film (but not too thin), breathe lightly on it and quickly lay it on the glass tubing in the dish from which the assistant has momentarily removed the lid for the purpose. He quickly replaces the lid and, when four similar preparations, each in its own dish, are ready, he takes them without delay to the incubator where the first will remain 15 minutes, the second 20 minutes, the third

25 minutes and the fourth 30 minutes. At each of those intervals a film is taken out, inspected to ascertain that it is still moist and allowed to dry in the air. Then it is stained in the usual way with Leishman or Giemsa stain. The count is made per 100 leucocytes, only the forms which show complete ex-flagellation being included. A count of total leucocytes per c.mm. in the peripheral blood is made at the time of taking the films in order that the number of ex-flagellating parasites may be expressed per c.mm. of blood as well as per 100 leucocytes.

"For *oökinetes* in blood from the mosquito's stomach.—Allow some female *A. maculipennis* without ripe ovaries to feed on a patient whose blood contains a good number of gametocytes and place them in a moist atmosphere incubator, the temperature being 25°C. and the humidity not less than 80 per cent. At intervals between 10 and 20 hours later remove one or two mosquitoes from the incubator and proceed as follows:—Chloroform the mosquito and remove its legs and wings. Flood the centre of a perfectly grease-free slide with Locke's fluid in which to dissect the insect. For dissection fix the left-hand needle on the thorax and with the right-hand needle nick the chitin on both sides of the fourth abdominal segment and gently pull on the last segment so as to draw out the mid-gut containing the blood clot without tearing the wall of the stomach. Using a dissecting microscope, cut away the malpighian tubules, lift the clot on the point of a dissecting needle and transfer it to a drop of Locke's fluid previously placed on another clean slide. Cut and tear the clot so that the blood as it leaves the stomach becomes quickly mixed with the Locke's fluid, but keep the teased area as small as possible to prevent any part of the blood from drying. When the blood and fluid are thoroughly mixed to form a large drop, make thin films from it on clean slides in the same way as if it were a drop of finger blood. With practice eight or more films can be made from the drop. Let the films dry in the air and stain with Leishman or Giemsa stain. Search for *oökinetes* with the oil-immersion lens." W. F.

GIOVANNOLA (Arnaldo). La colorazione vitale degli sporozoitii ed il suo impiego nella diagnosi dell'infettività degli anofeli. [**Vital Staining of Sporozoites in Anopheles.**]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 3. pp. 327-331. With 1 fig. English summary.

The author dissects anopheles in a 0.5 per cent. solution of brilliant cresyl blue in physiological salt solution [not 50 per cent. as in the English summary]. The sporozoites, which appear coloured and motile, are easily distinguished among the unstained fat droplets which come out of the thorax.

W. F.

TUDORANU (G.), HERESCU (D.) & GRINBERG (A.). Sur la lipase sérique chez les paludéens quininisés ou non quininisés. [**Serum Lipase in Treated and Untreated Malaria.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. pp. 1117-1118.

The serum lipase is not reduced in untreated malaria. When quinine is added to serum *in vitro* this fat-splitting lipase is destroyed, and when patients are treated with quinine or plasmoquine it is reduced. The quinine resistant corpuscle lipase does not pass into the plasma. W. F.

WINCKEL (Ch. W. F.). Kunstmatig opgewekte malaria quartana. [**Artificially Induced Quartan Malaria.**]—*Nederl. Tijdschr. v. Geneesk.* 1934. Sept. 29. Vol. 78. No. 39. pp. 4455-4475. With 3 figs. [12 refs.] English summary.

The inoculation of quartan malaria should be reserved for those patients who are immune to tertian. It is an excellent treatment when the paroxysms remain quartan, but the majority of the author's

patients had fever daily, or on three days out of four. The fever cannot be so readily controlled by drugs as the fever of tertian malaria; it is resistant to neosalvarsan. The incubation after mosquito bites, or after the subcutaneous inoculation of infected blood, averages 26 days. After intravenous injection it is only 10 days. Quinine acts perhaps a little more quickly than atebirin, but after atebirin there are fewer relapses.

W. F.

LACOUR (P. R.). *Recherches sur la malaria-flocculation de Henry.* (Sa sensibilité. Sa spécificité. Sa valeur pratique.) [**Henry's Malaria Flocculation.**].—67 pp. [80 refs.] 1934. G. Doin & Cie, 8 Place de l'Odéon, Paris (VI). [15 frs.]

The main conclusion is that the reaction is useful in diagnosis.

This little book begins with a description of the technique of Henry's reaction, the preparation of the iron and the melanin solutions, the arrangement of the tubes, and the reading of the results. This is followed by a review of the results obtained by HENRY himself, and by other workers. HENRY examined 100 healthy persons, all were negative; 450 persons with active malaria, all were positive except during the febrile attacks; 750 old malaria cases, many were positive; 400 syphilitics, all were negative. The findings of the other workers quoted were confirmatory. The author next gives the results obtained by himself in the examination of 381 sera. Twenty-eight cases of active malaria were all positive; 68 healthy persons were all negative. Two patients with sleeping sickness and 9 guineapigs infected with trypanosomes were all negative. Three patients suffering from haemolytic jaundice gave positive results; this appeared to be the only condition, except malaria, in which a positive reaction was obtained. The interval between the date of infection with malaria and the time at which the reaction became positive was studied in six cases of therapeutic malaria. The reaction in these patients was negative during the incubation, but became positive after five or six paroxysms had occurred. The author summarizes the views of HENRY, and of other workers, as to the nature and specificity of the reaction. His own view is that while this question remains unsolved, there is no doubt about the usefulness of the reaction in diagnosis.

W. F.

GREIG (E. D. W.), VAN ROOYEN (C. E.) & HENDRY (E. B.). **Serological Diagnosis of Latent Malaria.**—*Lancet*. 1934. June 30. pp. 1393-1394.

—, — & —. **A Note on the Melano-Precipitation Serological Reaction in Malaria.**—*Jl. Trop. Med. & Hyg.* 1934. July 2. Vol. 37. No. 13. pp. 193-195.

—, — & —. **Observations on the Melano-Precipitation Serological Reaction in Malaria.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 175-191. With 4 figs. [33 refs.]

The authors employ a pigment derived from hair, in place of Henry's antigen prepared from choroid membrane.

They have investigated Henry's melanoflocculation reaction in cases of induced therapeutic malaria. HENRY uses, as his antigen, a suspension of ox choroid membrane. A drawback to this melanin solution is that non-specific reactions may occur from the interaction of human

sera with the ox protein derived from the choroid. The authors therefore sought for a source of melanin pigment free from foreign protein and capable of reacting with malarial sera in a quantitative manner. This they claim to have found in pigment obtained from human hair.

"The melanin pigment solution is derived from human hair by hydrolysis with 50 per cent. HCl, followed by concentration in vacuo and purification by dialysis in a collodion membrane. This has been found to give a pure and stable suspension of pigment. A set of 9 dilutions of patient's serum is prepared ranging from 1:2 to 1:512 in distilled water. To each is added an equal volume (0.4 c.cm.) of pigment solution, and the series is incubated at 37°C. for 5½ hours before the reading is taken. Positive results are observed as white granular precipitates forming at the foot of the tube. . . The reaction appears about the 5th to 7th day of infection, although no parasites may be seen at this stage and the patient is afebrile. The maximum titre of 1:128 is reached about the 4th week, and then rapidly declines following the administration of drugs. Control tests on 129 different non-malarial sera gave only 2 non-specific positive results. It is probable that the phenomenon is not due to the interaction of antigen and antibody, for it can be shown that positively reacting sera may be inactivated by heating to 55°C. for half an hour and that the repeated immunisation of rabbits with melanin pigment fails to produce an agglutinin response."

The occurrence of a reaction with positive sera and dioxyphenylalanine, the precursor of melanin, shows that the reaction is due to the melanin and not to any other substance. [According to SINTON and GHOSH, malaria pigment, or haemozoin, is a different substance from the body pigment, melanin. See this *Bulletin*, Vol. 31, p. 706]. The lipoid phosphorus content of the serum tends to vary inversely with the reacting titre of the serum. The term melano-precipitation is suggested in place of Henry's melano-flocculation. W. F.

WISEMAN (R. Howitt). **The Nature of Henry's Reaction in Malaria.**—*Lancet*. 1934. Sept. 8. pp. 543-544.

This reaction can be obtained by adding distilled water to the serum; a solution of melanin is unnecessary. (See GREIG above, also CHORINE.)

The author employed the melano-precipitation method of Greig, van Rooyen and Henry, using their melanin solution prepared from hair (see above), and he made a parallel series of tests in which he used distilled water instead of melanin. He found that exactly similar precipitates occurred in both the distilled water series and the melanin series, the only difference being that the precipitate was coloured brown in the melanin tubes. Every case which was positive in the melanin tubes was positive in the controls with distilled water. HENRY calls the flocculation with distilled water "surflocculance." The author concludes "I have formed the opinion that these phenomena are one and the same, the melanin merely adding a brown colour to the flocculation. . . . The precipitate is in all probability a globulin." (See TRENSZ, this *Bulletin*, Vol. 30, p. 483.) W. F.

CHORINE (V.), PRUDHOMME (R.) & KOECHLIN (D.). Flocculation du sérum dans l'eau distillée et réaction de Henry. [**Henry's Reaction and the Flocculation of Serum in Distilled Water.**—*C. R. Soc. Biol.* 1934. Vol. 116. No. 27. pp. 1255-1257.]

The results obtained by adding sera to distilled water are almost exactly the same as those obtained with Henry's antigens (see WISEMAN above, also GREIG).

Normal sera give little or no flocculation in distilled water, syphilitic sera give a little flocculation, malarial sera give a great deal. The test is made by adding 0.2 cc. of the serum to 1.8 cc. of distilled water, and a reading is taken at once in the photometer. The tubes are then put in the incubator for 3 hours and, after 20 minutes at room temperature, a second reading is taken. The titre is obtained by subtracting the first reading from the second. A number of sera collected from normal persons, from syphilitics, and from people suffering from malaria were examined by this distilled water method, and simultaneously by Henry's melanoflocculation test. It was found that sera giving readings of less than 10 in distilled water gave negative Henry's reactions; sera giving readings between 10 and 25 gave doubtful Henry's reactions; sera giving readings above 25 gave positive Henry's reactions. Among 66 malarial sera, 60 gave readings between 35 and 60, 4 between 15 and 30, and 2 between 11 and 12. Among 130 syphilitic sera the readings were below 10 in 105. In 158 normal sera, the readings were below 10, and Henry's reaction was negative in 151. Among the remainder there were 7 (? 6) with readings between 10 and 15, three of these gave doubtfully positive Henry's reactions, and one with a reading of 21 gave a positive Henry's reaction. In kala azar, high titres of 100, 150 and more are reached.

The authors conclude that the flocculation of serum in distilled water and the reaction of Henry are due to the same principle, and that there exists an almost complete concordance between the two methods.

W. F.

GREIG (E. D. W.), HENDRY (E. B.) & VAN ROOYEN (C. E.). **The Chemistry of Malarial Serum, with Reference to the Factors concerned in the Melano-Precipitation Test.**—*Jl. Trop. Med. & Hyg.* 1934. Oct. 1. Vol. 37. No. 19. pp. 289-295. [12 refs.]

Melanin acts as an indicator in Henry's reaction, not as a true antigen. "Surflocculance" and flocculation with melanin are due to the same changes in the serum. (See CHORINE above, also WISEMAN.)

The authors have found that in sera giving a positive Henry's reaction there is no increase in albumen, total globulin, cholesterol or chlorides. The precipitate consists of one of the globulin fractions, probably euglobulin which occurs in excess in malaria. A positive reaction also occurs in kala azar, where there is also an excess of euglobulin. It is suggested that protolipoid complexes may enter into the reaction, since it cannot be merely a question of euglobulin increase, because this substance is in excess in syphilis, in which Henry's reaction is negative.

The authors have investigated the phenomenon of "surflocculance" or the apparent flocculation which occurs in tubes containing serum and distilled water without antigen. They conclude that this is probably the same as the flocculation which occurs with melanin solutions in Henry's reaction. The precipitation occurs in higher dilutions in the distilled water tubes than in the tubes containing melanin, and probably "the addition of the melanin solution has no effect other than that of suppressing the precipitation which would appear with a normal serum, and allowing only the deposition of the excessive amount of precipitate which comes down in a malarial serum. . . . There is a second use of the pigment, namely, to colour the precipitate and thus

make the reaction more easily observed, but this is relatively unimportant." The pH of the melanin solution is very important and a second factor of importance is found in the small quantity of sodium chloride which is present in it. "Both the slight alkalinity and the presence of this electrolyte will cause the suppression of any precipitate which would occur with normal serum on addition of water only," but the melanin solution does not contain enough alkali or chloride to suppress the larger reaction which occurs in malaria. Many other colouring matters can be used instead of melanin, *e.g.*, methyl violet, or methylene blue, but melanin gives the sharpest reaction. Melanin acts only as an indicator, and the active principles in the so-called "antigen" are the concentration of sodium chloride and the pH. (This *Bulletin*, Vol. 30, p. 483.) W. F.

CHWATT (L.). Influence de l'infection tuberculeuse expérimentale sur la réaction de Henry. [**Henry's Reaction in Experimental Tuberculosis.**—*C. R. Soc. Biol.* 1934. Vol. 116. No. 23. pp. 707-709.

The serum of tubercular guineapigs gives a positive Henry's reaction.

Two lots of guineapigs, one of 6 and the other of 4, were inoculated with a virulent strain of tubercle. Henry's reaction, which was negative at first, became positive in all of them during the third week, and remained positive until death, which took place 7 to 8 weeks later. With smaller doses, or with less virulent strains, the reaction may remain negative for months. The serum of 6 rabbits infected with syphilis gave a negative reaction. W. F.

HENRY (X.). La séroflocculation palustre. [**Seroflocculation in Malaria.**—*Arch. Inst. Prophylactique.* 1934. July-Sept. Vol. 6. No. 3. pp. 324-337. English summary.

The author describes the technique of his reaction, and the methods of preparing the reagents. He discusses the significance of the optic density as determined by Vernes's photometer. He states that if the serum is heated for half an hour at 55°C. specific flocculation no longer occurs, but that the flocculation of the serum with distilled water (surflocculation) is only slightly affected. [Some workers consider that surflocculation and melanoflocculation are essentially the same. (See CHORINE, WISEMAN, GRIEG above.)] W. F.

HENRY (A. F. X.). Les fausses flocculations en sérologie palustre. [**False Flocculation in Malarial Serology.**—*C. R. Soc. Biol.* 1934. Vol. 116. No. 27. pp. 1237-1239.

Anomalous positive reactions occasionally occur in other diseases than malaria. For instance, in typhus, trypanosomiasis, kala azar and tuberculosis of guineapigs. This is probably the result of a serological instability. True malarial flocculation is abolished when a serum is heated to 55°C. for half an hour. If flocculation occurs in a serum after it has been heated, one knows that it is not specific.

W. F.

DE MEILLON (Botha). **Entomological Studies. Studies on Insects of Medical Importance in South Africa.**—*Publications of South African Inst. Med. Res.* 1934. June. No. 33. pp. 249–308. With 16 plates.

The paper contains descriptions of new species of *Xenopsylla* and *Simulium*; of a new variety of *Anopheles natalensis*, differing from the typical form in the hypopygium and marking of the legs of the adult male and in the structure of the pupa; and of certain previously unknown early stages of South African *Anopheles*. The descriptions are fully illustrated.

Perhaps the most interesting part of the paper is the description of the eggs of ten species of *Anopheles*. The author finds distinctions between the eggs of *A. funestus* and of var. *leesoni*, and uses this knowledge to identify females caught in nature, dissecting them and examining the nearly mature eggs. He also finds that the egg of *A. cinereus* is peculiar in having no floats but hanging vertically in the water. In these points it resembles the egg of *turkhudi*; this is interesting, for the two species were known to resemble each other in the details of larval and pupal structure.

P. A. Buxton.

WASSILIEFF (A.). Quelques remarques sur les moustiques de Tunisie. [**Observations on the Mosquitoes of Tunis.**]—*Arch. Inst. Pasteur de Tunis.* 1934. Aug. Vol. 23. No. 3. pp. 368–383. With 1 folding map. [14 refs.]

Little, and that of a fragmentary character, has hitherto been published on the subject of this paper, which is of local rather than general interest. Notes are given on the larvae and breeding places, as met with by the author in the region to the south of the city of Tunis, of *Anopheles algeriensis*, *A. multicolor* and *A. hispaniola*. In the malarious district known as the Sahel de Sousse, numbers of paucidentate *A. maculipennis* females, usually gorged with blood, were found in a state of semi-hibernation in the larders of Arab houses. Such mosquitoes are especially dangerous, since they are capable of biting as many as thirty times; their destruction during the winter anti-mosquito campaign should therefore by no means be overlooked.

E. E. Austen.

GASCHEN. Prospection entomologique au Laos. [**Entomological Survey of Laos.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. May. Vol. 12. No. 5. pp. 533–540. With 1 fig.

As suggested by geology and climatology, the anopheline fauna of Central Laos, with which this paper is concerned, is the same as that of Tongking (excluding the delta). The component species are:—*Anopheles aconitus*, *A. aitkeni*, *A. barbirostris*, *A. fuliginosus*, *A. jeyporiensis*, *A. maculatus*, *A. maculipalpis*, *A. minimus*, *A. philippinensis*, *A. sinensis* and *A. vagus*. Among these, during the period 1931–1933, in the combined territories of Tongking, Annam and Laos, TOUMANOFF found much the highest percentage of infection (3.91) in *A. minimus*. This species occurs wherever the country is hilly or mountainous, and well watered. That *A. maculatus*, a possible vector, is ubiquitous in the Mekong valley is due to the periodic inundations caused by the river, and to the fact that this mosquito breeds in places freely exposed to the sun. Thus to prevent *A. maculatus* from breeding, shade rather than clearing is required.

A. culicifacies, not yet found in either the Lower or Central region, has been met with in Upper Laos. No specimen examined was infected, although in India an infection rate as high as 16 per cent. has been observed; special attention should be paid to this insect in Northern Indo-China.

Whenever it is desired to open up country for industrial development, a malarial survey, both clinical and entomological, should first be undertaken. Appropriate prophylaxis will then, in the words of ROUBAUD, rupture the relations between man and mosquito.

E. E. A.

ROZEBOOM (L. E.). **The Effect of Bacteria on the Hatching of Mosquito Eggs.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 496-501.

The author considers that results obtained by him, when working with eggs of the yellow fever mosquito (*Aedes aegypti*), may serve to reconcile discrepant findings of certain previous authors as to the influence of bacteria on hatching, since much depends on the age and condition of the eggs. When old and dry, eggs of *A. aegypti* rarely hatch in sterile water but, in the same medium, fresh, moist eggs do so much more readily. In the case of both dry and moist eggs the addition of bacteria has a stimulative effect on hatching. As previously stated by ROUBAUD (see this *Bulletin*, Vol. 27, p. 497), eggs deposited by older females tend to be "inactive." With regard to other species, the condition of the medium, whether sterile or contaminated, made no difference to the hatching of eggs of *Culex pipiens*, *C. territans* and *C. salinarius*.

E. E. A.

AMBALET (R.). Sur l'entraînement des larves de moustiques dans les cours d'eau. [**The Transportation of Larvae by Running Water.**]—*Arch. Inst. Pasteur d'Algérie.* 1934. June. Vol. 12. No. 2. pp. 205-208.

The author points out that it is possible for a collection of water to be free from larvae on one day and on the next to contain numbers of them in an advanced stage of development. He gives several examples. In a palm plantation at Biskra, the trees were watered once a fortnight. There was a hole in the ground at the foot of each tree. These holes communicated with one another, and when one was full of water it ran into the next, and so on. Most of the holes dried up in the interval between the waterings, but some retained a little water and in this mosquito larvae flourished. When the trees were next watered, these larvae were carried by the current and distributed among the other water-holes. Another example is given in which anopheline larvae were carried from a ravine into a water-hole in a vegetable garden.

W. F.

LEWIS (D. J.). **The Eggs of Four Species of Anopheles from West Africa.**—*West African Med. Jl.* 1934. Apr. Vol. 7. No. 4. pp. 135-136. With 1 fig.

The four species, the eggs of which were procured at Gadau, Northern Nigeria, are *A. gambiae*, *A. funestus*, *A. pharoensis* and *A. rufipes*, and Equatorial African specimens of all of these but the last were lately

described by GIBBINS [this *Bulletin*, Vol. 31, p. 56]. Eggs, readily obtained by the present author by isolating female mosquitoes in a suitably damp atmosphere, "were preserved on filter paper in sealed glass tubes wetted on the inside with a solution of five per cent. formalin and one per cent. glycerine." A short description is given of the egg of each of the above-mentioned species, accompanied by a table of measurements derived from the means of batches. Owing to the variability of anopheline eggs, it is, for diagnostic purposes, "necessary to examine eggs from large numbers of females." E. E. A.

TREILLARD (M.). Humidité et longévité dans la biologie et le pouvoir pathogène, en Indochine méridionale, de *Myzomyia minima* et *Pseudomyzomyia vaga*. [**Humidity and Longevity in the Biology and Pathogenic Power of *Anopheles minimus* and *A. vagus* in S. Indo-China.**—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 668–670.]

A. minimus is the chief malaria carrier in Indo-China, but *A. vagus*, one of the species in which the plasmodium is least often found, is said to be definitely zoophile. Apart, however, from the different degrees of androphily displayed by these two species, the harmlessness of *A. vagus* to man is explicable by the shortness of its life as compared with that of *A. minimus*. It is obvious that the longer a domestic *Anopheles* survives the greater will be its chance of conveying malaria by biting a second time. In artificial conditions the mean duration of life is about five times longer in *A. minimus* than in *A. vagus*, and in both cases individual longevity is most marked at the time of greatest abundance—the dry season for *A. minimus*, the rains for *A. vagus*. At the seasons indicated, the former breeds in clear streamlets, the latter in collections of waters heavily charged with organic matter. Thus differing longevity would seem to be associated with a fundamental difference in larval nutrition, since shortness of life characterizes individuals reared on material rich in protein, and markedly longer life those brought up in a medium poorly supplied with vegetable food.

The difference in the seasonal occurrence of the two species would appear also to be due to the different hygrometric requirements of their respective adults, a high degree of prolonged humidity being unfavourable in the one case, while the lack of it is even more so in the other.

E. E. A.

MANSON (D.). **Some Notes on the Identification of Some Anopheline Larvae by Macroscopic Methods.**—*Records of the Malaria Survey of India.* 1934. June. Vol. 4. No. 2. pp. 197–203.

The author has found that practice has enabled him to identify anopheline larvae in the field with a considerable degree of accuracy by putting them in a white porcelain dish and examining them with the naked eye. A table is given which sets out the distinguishing points of 18 species of anopheline larvae. W. F.

BOYD (Mark F.) & MULRENNAN (J. A.). **The Establishment of a Cage Colony of *Anopheles punctipennis*.**—Reprinted from *Ann. Entom. Soc. America.* 1934. June. Vol. 27. No. 2. pp. 311–312.

Stimulated by their success in maintaining a colony of the North American *A. quadrimaculatus* for more than two years, the authors, in

Florida and using the same technique, turned their attention to *A. punctipennis*. Having, down to the end of March, 1934, raised three generations of the latter, they are satisfied that they have established a colony capable of reproducing itself indefinitely. It is noted that, in the insectary, a negro is attacked by *A. punctipennis* more avidly than is a white man; and that, while *A. quadrimaculatus* is prone to bite the legs, the upper parts of the body are preferred by *A. punctipennis*.
E. E. A.

COMPAGNINI (G.). Cambiamento dei caratteri somatici della fauna anofelica nella bonifica di S. Eufemia. [**Change of Somatic Characters of Anophelines after Bonification.**]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 3. pp. 264–271. With 1 map. English summary (10 lines).

In the bonificated region of South Eufemia, zoophilous multidentate anopheles (average number of dentations more than 14) were most common in those places where animals had been kept in stables and where the ground had been developed by agriculture for some time prior to the installation of great drainage schemes; but in the regions where hydraulic works of sanitation had been carried out without previous cultivation of the land, there was a striking prevalence of the androphilous paucidentate variety.
W. F.

NIJKAMP (J. A.) & SWELLENGREBEL (N. H.). Waarnemingen hoe *Anopheles maculipennis* den nieuwen Wieringermeerpolder binnen-drong. [**How *Anopheles maculipennis* invaded the New Wieringermeer Polder.**]—*Nederl. Tijdschr. v. Geneesk.* 1934. July 28. Vol. 78. No. 30. pp. 3427–3443. With 3 figs. & 1 graph. English summary.

SWELLENGREBEL (N. H.) & NYKAMP (J. A.). **Observations on the Invasion of the Wieringermeerpolder by *Anopheles maculipennis*.**—*Quarterly Bull. Health Organisation, League of Nations*. Geneva. 1934. Sept. Vol. 3. No. 3. pp. 441–460. With 4 maps & 1 chart.

The observations described were made in Holland from 1931 to 1933. In the Wieringermeer, as in other sea polders (low-lying reclaimed land), the high salinity of the water prevents *A. maculipennis* from breeding, but this obstacle will gradually disappear. Meantime the local anopheline density is only one-fourth or one-fifth of that in areas where breeding is unhindered, and the greater part of the adult Wieringermeer Anopheles is composed of immigrants. As a set-off, since rabbits and poultry form the only livestock, there is little "stabular deviation," and the mosquitoes are very numerous in houses. Although mosquitoes in bedrooms, and therefore potential malaria-carriers, were regularly destroyed, the numbers of Anopheles found in each house were scarcely affected. More energetic measures, however, especially the use of pyrethrum sprays, consequent on the appearance of malaria in the new polder, caused wholesale destruction of the domestic, immigrant Anopheles. Yet unless stabular deviation be established concurrently with breeding conditions, when the latter become normal, malaria is likely to be more prevalent in the Wieringermeer than in districts outside.
E. E. Austen.

DE BUCK (A.) & SWELLENGREBEL (N. H.). **Behaviour of Dutch *Anopheles atroparvus* and *messeae* in Winter under Artificial Conditions.**—*Riv. di Malarologia*. Sez. I. 1934. Vol. 13. No. 4. pp. 404-416.

The authors' summary is as follows :—

"*Atroparvus* in winter requires occasional bloodmeals to keep alive, *messeae* does not. The natural winter habits of *atroparvus* and *messeae* can be changed completely by artificial conditions (high temperature and humidity, over-feeding). These conditions remove the physiological difference between the two races during natural hibernation : gonotrophic dissociation in *atroparvus*, gonotrophic concordancy in *messeae*. But this physiological difference remains, none the less, a very real one as the natural behaviour of an animal is, obviously, of more importance than its reactions to artificial conditions it is not likely to meet in nature."

W. F.

DE BUCK (A.), SCHOUTE (E.) & SWELLENGREBEL (N. H.). **Cross-breeding Experiments with Dutch and Foreign Races of *Anopheles maculipennis*.**—*Riv di Malarologia*. Sez. I. 1934. Vol. 13. No. 3. pp. 237-263. With 6 figs. on 1 plate.

While the details of the lengthy series of experiments described in this paper are of much interest from the Mendelian standpoint, the practical outcome may well be that, at least in the majority of cases, what are now regarded as varieties, races or sub-species of *A. maculipennis* will henceforth rank as distinct species. According to the authors the "most important conclusion", to be drawn from their studies, "is the proof that the Dutch races of *Anopheles maculipennis*, which in the course of the last 9 years have been recognised as units, can claim to be considered as species from a genetic point of view, because they maintain their independent status in nature by their interracial sterility. *Atroparvus*, moreover, has to be assigned a position quite apart from all known races of *Anopheles maculipennis* on the strength of its stenogamy (mating in confinement)."

E. E. Austen.

WEYER (Fritz). Ueber die Anophelen Mecklenburgs, insbesondere die Verbreitung der Rassen von *Anopheles maculipennis*. [**The *Anopheles* of Mecklenburg, especially the Distribution of the Races of *A. maculipennis*.**—Reprinted from *Sitzungsberichte u. Abhandlungen d. Naturforschenden Gesellsch. z. Rostock*. 1933. 3rd Ser. Vol. 4. pp. 59-75. With 3 figs.

The Anopheline fauna of Mecklenburg consists of *A. maculipennis* (generally distributed, and including the races *atroparvus*, *messeae* and *typicus*), *A. bifurcatus*, *A. plumbeus* and *A. algeriensis*, the latter met with in one locality and previously only twice found in Germany.

*Details of the local occurrence of the races of *A. maculipennis* are given, and its causes are discussed. The dominant coastal form is *atroparvus*, a more adaptable race than *messeae*, the peculiarities of which it sometimes exhibits; both *typicus* and *messeae* occasionally oviposit on brackish water. From year to year and at different seasons of the same year, chiefly as a result of climatic and temperature changes, the proportions of the three races in local mosquito populations show marked variation. Although in Germany, as in Holland, where

malaria occurs *atroparvus* predominates, this in itself is not a sufficient justification for describing the latter as a "dangerous" race. On the contrary, it need not always be associated with malaria; and on the coast of Mecklenburg, as in the marshes of the Elbe and certain other localities where *atroparvus* abounds, the absence of malaria cannot simply be ascribed to the presence of a particular race, or to a peculiar property of the latter. E. E. A.

HACKETT (L. W.). **The Present Status of our Knowledge of the Sub-species of *Anopheles maculipennis*.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 109–128. With 3 plates. [35 refs.]

To the reader well-nigh swept off his feet by the present spate of papers dealing with the racial question in *A. maculipennis*, this clearly written résumé will furnish a welcome holdfast.

Wing-measure and maxillary index, as well as certain larval hairs and a spine on the male hypopygium show divergences from the mean, and we have to fall back upon egg-characters. In Europe, the bulk of *A. maculipennis* is readily divisible according to the design on the dorsal surface of the egg into five groups, or six if *A. elutus* be regarded as a sub-species. The diagnostic characters of these six groups, races, varieties or sub-species are conveniently shown in a table. That the features exhibited by the eggs are really of value, for the distinction of groups or sub-species, is indicated by the fact that larvae and adults bred from a given type of egg exhibit a combination of distinctive characters—morphological, statistical and biological.

The local occurrence of a given sub-species, within its range, would seem to depend primarily upon the nature of the water in potential breeding places. On the other hand the various types of egg are apparently connected "not only with an adaptation to certain kinds of breeding place, but also with other physiological characters of the sub-species, as exhibited in sexual behaviour and winter habits."

Although no race of *A. maculipennis* actually shuns man, wherever there is livestock more hungry mosquitoes are attracted to the animal than to human habitations. Thus, instead of "deviation by animals," we should more properly speak of occasional deviation by man. The reasons, whether chemical or physical, for the higher attraction of animal quarters are obscure.

The limited endemicity of malaria in Holland and N. Germany (E. Friesland), although the distribution of the proved carrier (sub-sp. *atroparvus*) is much wider, probably results from the effect of certain factors upon the attraction of domestic animals. "The ability of any local anopheline population to maintain malaria depends on the degree to which it uses human beings as host." E. E. A.

FEDERATED MALAY STATES. **Annual Report of the Malaria Advisory Board for the Year 1933** [MARTIN (P. H.), Acting Chairman].—16 pp. 1934. Kuala Lumpur: Govt. Press.

The Board approved unanimously a resolution to the effect that, after considering the question of drug prophylaxis, they desired to emphasize their opinion that no available method could be regarded as a satisfactory substitute for anti-larval control. A low grade oil made from the residue of finer grades, and known as Sludge Oil, was found to be

unsuitable for antimalaria purposes. Reports were received that water contaminated with oil caused the death of fowls, but experiments made by the Board showed "that antimalarial oiling was of no great danger to poultry."

A sub-committee reported to the Board on the subsoil drainage of Terentang Estate, a government-subsidized experiment which had been going on for many years. They concluded that "this experiment could not be taken as satisfactory evidence either for or against the use of subsoil drainage on estates." They found that the designing and laying of subsoil drains required more expert knowledge than is available among the staff of an estate; but that the knowledge necessary for keeping such drains in repair could be acquired readily. The cost of upkeep on estates is greater than on cleared sanitary board areas. "Provided such specialized supervision were available, there is no reason to suppose that anti-malarial subsoil drainage would not be as successful on estates as elsewhere." As regards the question of costs, compared with other equally adequate anti-malarial measures, it was felt that, as so much depended upon local factors, no definite pronouncement could be made.

Professor K. B. WILLIAMSON had reported to Board on the efficacy of sluicing as a method of larval control in Cameron Highlands, and they had conducted experiments in lowland ravines selected by him, and provided with sluice-gates made to his design. The friable soil of the lowlands rendered the method unsuitable. Heavy rain repeatedly washed away the gates and, apart from this, the flush of water when the gates were opened damaged the banks. In addition, it was found that "destruction of larvae which remain stranded within the reservoirs and drains cannot be assured." W. F.

ARNELL (O. R.). **The Control of Malaria.**—*East African Med. JI* 1934. Sept. Vol. 11. No. 6. pp. 200-202.

In his report on the prevention of malaria in Mauritius (1908) Sir Ronald Ross first attempted to formulate the quantitative laws describing the rise and fall of malaria in terms of variations of the natural factors (frequency of anophelines, proportion of cases of malaria at a given moment, etc.). On Sir Ronald's suggestion, Mr. H. WAITE published a mathematical study of the problem in 1909-10 (*Biometrika*, Vol. VII, p. 421) and finally Sir Ronald himself dealt with the subject at length in an addendum to the second edition of *The Prevention of Malaria*. Mr. Arnell's article discusses the subject very briefly, and offers, without proof, a formula expressing the malaria rate in terms of nine variables. It would be impossible without close study to say how far the result is an improvement upon that reached by Ross. M. Greenwood.

VICKERS (W. J.), WEST (G. F.) & D'NETTO (S. G.). **Economy in Large Scale Antimalarial Control in Kuala Lumpur, Federated Malay States.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. June 30. Vol. 28. No. 1. pp. 85-99. With 1 fig. [18 refs.]

—. **Some Recent Local Advances in the Economics of Practical Malarial Control.**—*Malayan Med. JI* 1934. June. Vol. 9. No. 2. pp. 40-43. [32 refs.]

The new brush-oil-spray method adds to efficiency and greatly reduces the costs. Paris green is not as good as oil. Fish are useless. Brushwood is washed away in wet weather.

The official boundaries of Kuala Lumpur, the capital of the Federated Malay States, enclose an area of 16 square miles with a population of 120,000. The official anti-malaria zone extends for half a mile beyond these boundaries and comprises an area twice as large. Permanent anti-malaria work is carried out by the P.W.D. and consists of efforts to remove all water as quickly as possible by means of concrete surface drains and subsoil pipes. About one-third of the area is controlled in this way, the rest is still under earth ditching and oiling, the so-called temporary larval control. Oil was applied every 7 days up to 1933 and the results were very satisfactory; the numbers of fresh cases arising in the town were 37 in 1929, 83 in 1930, 45 in 1931, 36 in 1932; with a spleen rate of 1 to 4 per cent. in the children. It became necessary in 1933 to make large reductions in expenditure; several ways of reducing costs were tested experimentally, such as extending the intervals between successive oilings and so on, but the most satisfactory results were obtained by a modification of Quaife's method of brush oiling (see this *Bulletin*, Vol. 31, p. 711). A thin line of oil is sprayed on the surface of the stream or drain with an oil-sprayer, and then a coolie distributes it vigorously with a brush for a 100 yards or more down the stream. All large ponds are similarly treated at the edges and all small ponds and pot-holes are treated with a mop dipped in oil. It is unnecessary to oil the main channels, because enough reaches them from the side streams. The authors emphasize "that in such a scheme as the above, where a minimum of oil is used, grave danger will be encountered unless *constant, skilled and intimate supervision* is possible. In Kuala Lumpur this is obtained only through a thoroughly trained oiling and maintenance gang. . . . Better and more systematic upkeep of drains is required with this method than with the old." The average cost per annum of oiling a drain 3 feet wide by the old spray method was \$1.31, the cost with the new brush-spray method was only \$0.88. The results, as regards the prevention of malaria, by the new method have been excellent. The number of fresh infections in 12 months has been reduced to 24, and the spleen rate has fallen to 0.73 per cent. The oil used is the M.D.B. mixture of the Asiatic Petroleum Co., consisting of solar oil 45 gallons, Diesel oil 15 gallons and kerosene 4 gallons.

As regards some other methods of control, such as fish, the authors state that in their experience the natural enemies of larvae "are rarely of practical value." Paris green is as costly as oiling and, in Kuala Lumpur, the results are less satisfactory. Brushwood (see this *Bulletin*, Vol. 31, p. 712) is of value in preventing anopheline breeding, but it is washed away in heavy rain, and overflow and seepage result unless the drains are taken to a depth at least three times that normally required.

W. F.

STRICKLAND (C.) & GIBSON (D.). "Backdoor Drainage," an Anti-malarial Measure designed to meet a Particular Physiographical Situation in Sylhet District, Assam.—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 432-437. With 2 maps & 9 figs.

Swamps, or *bhils*, are frequently formed when the mouth of a tributary stream becomes silted up. "Back-door drainage" apparently means the cutting of a channel which drains the *bhil* in a direction different from that of its original outflow.

"The common practice of the straightening out of rivers by cutting by-passes is folly, because as explained above, rivers are curved in their courses in obedience to dynamic laws; . . . on no account should open drainage through recent alluvium be resorted to, but such areas of deterioration may perhaps be drained out by the 'back-door method,' thus defeating nature by a stratagem. This back-door drainage is very often impracticable, as a cutting to an active stream at a suitable level would be too costly."

W. F.

MURPHY (R. A.). **Anti-Malarial Work on a Group of Tea Estates in South Sylhet.**—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 437-439. With 1 chart.

In 1926, practically no anti-malarial work had been attempted in the tea districts in India, and consequently the scheme which was based mainly on the findings of Dr. STRICKLAND in his survey of tea districts in 1922-23 was really an experiment in sanitation. The estates lie on low hills bordering the flood plains and their drainage is obstructed by alluvial deposits. The first step was to deal with the extensive anopheles-breeding marshes or *bhils*. This was accomplished by silting or by "back-door" drainage (see STRICKLAND above). The next step was to deal with the drains; this was done by growing shade trees and shrubs along their banks. Cattle do much damage to the growing vegetation and it is necessary to prevent this by fencing. On the whole the results to health have been very satisfactory. In one garden, the August sick-rate has dropped from 19.6 per cent. to 2.5 per cent., and this may be claimed as fairly typical of the results obtained.

W. F.

WHITE (R. Senior) & ADHIKARI (A. K.). **Anti-Gametocyte Treatment combined with Anti-Larval Malaria Control.**—*Records of the Malaria Survey of India.* 1934. June. Vol. 4. No. 2. pp. 77-94. [16 refs.]

A single course of quinine and plasmoquine given at the beginning of the malaria season to all the children living in an area under anopheline control caused no permanent improvement.

The Railway Settlement of Dangoaposi has been under malaria control ever since the epidemic which marked the opening of the line in 1925. The rice-fields have been treated with Paris green since 1930, because it was found that *A. culicifacies* bred in puddles in those portions which lay fallow. The object of the experiment here described was to determine whether the good results already obtained could be improved by an antigametocyte treatment. Each child was given a ten-day course of euquinine with 5 days of plasmoquine in the middle of the course. The average daily doses for children between 7 and 10 were 7.4 grains of euquinine and 0.012 gram of plasmoquine. Toxic symptoms appeared in two cases. The immediate effect of the treatment was to cure 53 per cent. of the benign tertian and 85 per cent. of the subtertian cases, and also to remove 83 per cent. of the gametocytes. But, by the end of the season, the numbers of infections and the numbers of gametocyte carriers were as high as at the beginning of the experiment. "It is therefore obvious that, even with a high degree of efficiency in anopheline control, no additional good is to be looked for by a single attack on the gametocyte carriers at the commencement of the season."

W. F.

ROBIN (L. A.). Résultats pratiques de la prophylaxie antipalustre en général et de la lutte antilarvaire en particulier sur quelques exploitations agricoles en Indochine méridionale. [**Malaria Prevention on Estates in Southern Indo-China.**]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Apr. Vol. 12. No. 4. pp. 378-401. With 8 graphs & 4 plates.

—. Ce qu'il faut entendre par "assainissement spontané" des plantations en Indochine méridionale De la prémunition chez l'adulte. [**The Meaning of Auto-Sanitation of Estates. Premunition.**] *Ibid.* pp. 402-421. With 3 graphs.

Antilarval methods are necessary.

The author gives a number of graphs and diagrams showing how malaria has been successfully combated on rubber estates in Indo-China. Quinine prophylaxis prevents illness from malaria and greatly reduces the daily sick-rate. For example, on an estate where 0.5 gram was given daily, the sick-rate was reduced from 30 to 17 per cent. in 6 months and the death rate from 5 to 2.2 per cent. Prophylactic quinine is not satisfactory however, because it does not reduce the number of infections; on this same estate during the same period the splenic index increased from 75 to 92 and the parasitic index remained unredacted at about 60 per cent. (see LACAUX below). Under such conditions any relaxation of supervision means an outbreak of illness. Malarial infection on such an estate can be effectively reduced only by combining antilarval measures with the quinine prophylaxis. By this means the splenic index was reduced 50 per cent. in six months and the parasitic index even more.

On some estates where reliance was placed solely upon prophylactic quinine, malaria increased to such an extent that the land was abandoned; but in other cases, the terrible losses from malaria gradually became less and, after a few years, although nothing had been done, the estates appeared to have effected their own sanitation. Several examples are given, where the sick rate was only 3 to 10 per cent., but on examination it was found that the splenic index was about 84 per cent. and the parasitic index nearly as high. The improvement was not due to eradication of infection, but to premunition, that is an acquired tolerance on the part of the adult coolies which was associated with latent infection. The non-immune children suffered severely; the birth-rate was low, the infantile deaths and the abortion rates were high. This condition of equilibrium is reached in about 5 years, provided fresh labour is not imported. The arrival of new, non-immune coolies on such an estate means a fresh outbreak of malaria. From every point of view, humanitarian, political, and financial, antilarval measures combined with the judicious administration of quinine should be employed on rubber estates situated in the malarious regions of Southern Indo-China.

W. F.

ROBIN (M.). La prophylaxie antipaludique dans les plantations de l'Indochine Méridionale. La lutte antilarvaire. Son efficacité. [**The Prevention of Malaria in the Rubber Estates of Indo-China.**]—*Bull. Soc. Path. Exot.* 1934. July 11. Vol. 27. No. 7. pp. 691-699.

Antilarval measures succeeded where quinine and improved general sanitation had failed.

The author gives a number of instances of the calamities due to malaria which occurred when rubber estates were being opened in virgin jungle and labour was being imported. In one plantation 200 coolies out of a total labour force of 650 died during the first year. The removal of the whole village from the marsh where it was situated to high ground some distance away made but little difference. Prophylactic quinine did not lower the rate of infection; the few children born on the estate died in infancy. Antilarval work was then undertaken by means of open drains and oiling. When the drains were finished in July 1929, the daily average sick rate was 20 per cent. of the labour force; by September it had fallen to 15 per cent., and throughout 1930 it was only 2.5 per cent. On another estate where antilarval measures were equally successful and where the daily sick-rate was reduced from 15 to 4 per cent. within a year, the transfer of the manager, and consequent withdrawal of European supervision, resulted in a return of malaria, and a few months later the sick rate was as high as ever.

W. F.

FARINAUD (E.). Un exemple de prophylaxie antianophélienne : Tri-cu. [**Anti-Anopheline Prophylaxis at Tri-cu.**].—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Mar. Vol. 12. No. 3. pp. 345-360. With 1 chart & 3 figs.

— Essai de prophylaxie rationnelle du paludisme en milieu infantile à Tri-Cu (Tonkin).—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 568-575.

Amelioration produced by brush-oiling.

An outbreak of malaria occurred in a kind of reformatory for children at Tri-cu. As a measure of urgency a daily dose of quinine was given. This stopped the fatalities and most of the sickness; the children were able to resume their agricultural employment, but the parasite and spleen rates were still high. Drainage and oiling by Quaipe's brush method (see VICKERS, above) brought about a great improvement.

W. F.

LACAUX (J.). Que pensez-vous de la quinine ? [**What of Quinine ?**].—*Rev. Méd. et Hyg. Trop.* 1934. May-June. Vol. 26. No. 3. pp. 154-159.

The successful employment of prophylactic quinine on rubber estates.

The author's observations as to the value of prophylactic quinine on a number of estates in Indochina, employing altogether 35,000 coolies, are as follows :—(1) Where no prophylactic quinine is given, the proportion of sick may reach 80 per cent. (2) Where quinine is given intermittently the daily sick rate is about 30 per cent. (3) Where it is given regularly the figure is 12 per cent. (4) Where regular quinine is combined with destruction of anopheline breeding places malaria disappears, as, for instance, on the Michelin rubber plantations at Dao-Tieng and Phow-Rieng in Cochin-China.

W. F.

HENDERSON (L. H.). **Prophylaxis of Malaria in the Sudan, with Special Reference to the Use of Plasmoquine.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Aug. 4. Vol. 28. No. 2. pp. 157-164. With 6 graphs.

The best results were obtained with a small bi-weekly dose of plasmoquine as an adjuvant to anti-larval operations.

The Gezira is the extensive cotton growing area of the Sudan ; it is a stretch of flat land 700,000 acres in extent along the west bank of the Blue Nile. The malaria season is from September to January, and it is just at this time that the cotton fields are irrigated. The maximum rainfall is in July. The carrier is *A. gambiae*. Little breeding occurs until September ; it is then almost synchronous with the rapid increase of malaria which occurs during that month. The chief method of prophylaxis is extremely active anti-larval measures, but this work is complicated by the necessity for artificial irrigation of the growing crops during the most malarious period of the year. The author therefore decided to see what could be accomplished by means of plasmoquine. An isolated group was treated with quinoplasmine for a fortnight, at the end of which time parasites were found in only one. For the next 3 months, each adult was given 0.02 grams of plasmoquine simplex daily with half doses for children. During the first part of the time there was a considerable reduction in the incidence of malaria, but towards the end the parasite rate rose to almost the same height as in the control group, though the general health of the treated group was greatly improved and very few showed symptoms of clinical malaria. A second series of experiments was carried out in boys' schools ; here 0.02 gram of plasmoquine simplex was given twice a week, for a period of ten months, with the object of destroying the gametocytes. During the time that the treatment lasted, gametocytes practically disappeared from the blood, there was a considerable reduction in the amount of malaria and the general health of the boys was greatly improved. After the cessation of the treatment, all these good results gradually disappeared, and when the schools were revisited a year later, conditions were much the same as they had been before it was carried out. No toxic symptoms were caused by the plasmoquine. The author concludes that " small daily doses of the drug for causal prophylaxis are not recommended as they tend merely to conceal infection. The results of experiments in gametocyte prophylaxis tend to show that a bi-weekly dose of 0.02 gramme plasmoquine simplex to children might be of value in anti-malarial work."

W. F.

LEGENDRE (F.). Expériences de projection de poudres larvicides par avions à Madagascar. [**Larvicidal Powder spread by Aeroplanes in Madagascar.**]*—Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 603-608.

Paris green was spread by low-flying military aeroplanes over marshes and rice-fields in the environs of Antananarivo. Though this by no means destroyed all the larvae, it secured an appreciable diminution in the number of mosquitoes.

W. F.

RUSSELL (Paul F.) & EATON (L. S.). **An Automatic Distributing Machine for Paris Green Mixtures.***—Philippine Jl. Sci.* 1934. Apr. Vol. 53. No. 4. pp. 497-503. With 2 figs. & 2 plates.

This paper describes an automatic distributing machine for Paris green which is driven by the stream in which the larvicide is to be distributed.

W. F.

PECKOLT (Waldemar) & PRADO (Alcides). Ensaio da acção larvívica do *Enterolobium timbouva*, Mart., (Leguminosae), na prophylaxia culicídica. [*Enterolobium timbouva* Mart., as a *Culicicide*.]—*Ann. Paulist. Med. e Cirurg.* 1934. Sept. Vol. 28. No. 3. pp. 261–263.

Enterolobium timbouva is a tree known to be poisonous for cold-blooded animals, and is used by the natives for poisoning fish. It thrives in Rio de Janeiro and the southern States of Brazil. Its wood and bark contain a saponin which with water or alcohol, in either of which it is readily soluble, forms a sapotoxin.

A table gives the results of some experiments on its use as a larvicide and shows that it is rather less effective than Paris green. H. H. S.

JATSENKO (F.). [*The Use of Chlorpicrine as a Mosquito Larvicide*.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 1. pp. 91–93. [In Russian.]

In an attempt to find cheaper substitutes for Paris green the author conducted a series of field experiments with various substances. The present paper records the results obtained with chlorpicrine.

Chlorpicrine can be employed against mosquito larvae (1) as a fumigant, and (2) as an intestinal poison. In the first case, chlorpicrine in the proportion of 1 litre per 1 hectare of water surface is mixed with 1 kilogram of fine road dust and 2 litres of paraffin oil, the mixture being kept in a well-closed receptacle for 4–6 hours. Just before being used it is mixed again with dry road dust, the whole mass is placed in a pulverizer and sprayed over the surface of the water. This treatment results in the destruction of 100 per cent. mosquito larvae, pupae and eggs, as well as of some other aquatic animals, in 24 hours. Fish are affected only when the depth of the water does not exceed 12–15 cm. Owing to the harmful action of chlorpicrine upon the eyes, human beings and cattle should be kept away from the area under treatment for about 2 hours. When used as an intestinal poison, 100–150 grams chlorpicrine are mixed with 1 kilogram of flour, 1 kilogram of fine road dust and 100–150 grams of paraffin oil, the total amount being the dose per 1 hectare. The mixture is kept for 24 hours in a closed vessel after which it is again mixed with 4 or 20 times its weight of dust (according to whether it is spread by means of a pulverizer or by hand respectively). By this method all mosquito larvae (but not their eggs or pupae) can be destroyed in 10–12 hours. The use of chlorpicrine as an intestinal poison has certain advantages over its use as a fumigant: (1) a smaller amount of it is required, (2) its action upon the larvae is more rapid, (3) it can be applied by hand. However, in other respects the first method is superior. C. A. Hoare.

KUTCHER (S.). [*Anthracene—a New Mosquito Larvicide*.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. pp. 141–148. [In Russian.]

Experiments were conducted with the object of testing the effect of anthracene upon mosquito larvae, using the refuse of coke-benzole works containing about 12–15 per cent. pure anthracene. The best results were obtained, both under laboratory conditions and in the field, with a mixture of this substance and dust containing 10 per cent.

anthracene. The mixture is spread over the surface of the water by means of a pulverizer. Repeated tests showed that practically 100 per cent. mosquito-larvae (anopheline and culicine) are destroyed by this method. Since about 900 tons of the anthracene-containing substance are thrown out monthly in the Ukraine, this industrial refuse represents an economical substitute for Paris green. Its effect upon fish and water-vegetation has not been determined. C. A. Hoare.

BROWN (J. Youngson). **Safe Mosquito Nets for Use in Nigeria.**—*West African Med. Jl.* 1934. Apr. Vol. 7. No. 4. pp. 147-148.

Netting of 25/26 gauge was found sufficient to exclude mosquitoes.

These experiments were undertaken to determine if it would be possible to exclude mosquitoes by a net of larger mesh than the 42/44 mesh in common use, and to increase ventilation and comfort without sacrifice of efficiency. A rectangular box was divided into two compartments by a removable frame upon which pieces of mosquito netting of differing mesh were stretched and tested, mosquitoes were put in the box on one side of the netting and a guineapig was put in on the other side. A netting of 25/26 gauge was sufficiently fine to prevent the passage of mosquitoes and this was confirmed by its use in the field. W. F.

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REVIEWS AND NOTICES.

ASHFORD (Bailey K.). **A Soldier in Science. The Autobiography of Bailey K. Ashford.**—425 pp. With 4 plates. 1934. London: George Routledge & Sons Ltd. Broadway House, 68-74 Carter Lane, E.C.4. [12s. 6d.]

Bailey Kelly Ashford died on 1st November, 1934, the date of publication of this autobiography. Of Devon stock on both sides, he was son of the Professor of Surgery and later Dean of the Medical School at Georgetown who was called in too late when President Garfield was shot, and who had fought for the South in the Civil War. Influenced by his striking personality, Ashford decided on the U.S. Army Medical Service as a career. The Spanish American war took him to Porto Rico, where he married Maria Anuncion Lopez, daughter of the Marques de Villar, a republican in spite of his title. Ashford was stationed at Ponce when it and its surrounding district was devastated by the hurricane on San Ciriaco's day, 8th August, 1899, and which left homeless 800,000 persons for the army to keep alive. It was the finding that these starving anaemics did not get better with good food that led to his discovery of eosinophilia in their blood and hookworm eggs in their stools, and to the now famous telegram to his superior announcing that he had proved that many of the pernicious progressive anaemias of Porto Rico were due to hookworms. It is true that in French and German handbooks on zoology and on historical and geographical pathology the presence of hookworms had been recorded before 1883, but the local knowledge of this is sufficiently shown by the volume of local ridicule, medical and lay, which met Ashford's announcement that the anaemia from which the jíbaro [peasant] so terribly suffered was due to a worm and not to malnutrition. Ashford's reduction by thymol treatment of the island's mortality from anaemia by 85 per cent., with its increase of the jíbaro's earning capacity by 60 per cent., proved convincing to opponents. The book tells how Ashford was enabled to reach the position to do this by obtaining the headship of a Commission to investigate this point. As is so well known there followed a notable campaign admirably executed.

As to the details of its repercussions in the United States, STILES writes to the reviewer that Ashford's memory is to some extent at fault. When Mr. Rockefeller's office agreed to put up a million dollars for hookworm work in the South, it was insisted that STILES should resign Government Service to give his whole time to administering the fund. Having agreed to the resignation, STILES proposed that the work should be divided into administrative and scientific sides. He was appointed scientific secretary and upon consultation with Walter Page, later Ambassador in London, suggested J. Y. Joyner as administrative secretary; and when, after the announcement of Mr. Rockefeller's gift had been made, he refused, Page shortly after selected Wickliffe ROSE in that capacity. That is to say the hookworm campaign was determined upon before ROSE joined its staff. So, too, does Ashford's memory appear to have been at fault as to the handing over for description to HASSALL, Stiles's assistant, of his original specimens of hookworms from Porto Rico, Ashford having recognized that they could not be *Ancylostoma duodenale* since they had "no front teeth." The specimens are in the Army Medical Museum. Although in the interests of medical history these statements have to be made, they do not affect in any way the magnificent work which Ashford did.

In entertaining fashion Ashford tells of his various delegations to Europe, Brazil, Cuba, Dominica and Egypt (in the last he received from King Fuad the Grand Cordon of the Order of the Nile), and his responsibilities for American troops in France during the Great War. Nearly a third of the book is taken up with this last. He was with the first division which left America, and in France had command of the school at Langres for the battle training of all medical officers of the A.E.F. He obtained the D.S.M. and Honorary C.M.G., and on recall to Washington became Editor in Chief of the United States Medical History of the War. His other main administrative work was the founding of an Institute of Tropical Medicine and Hygiene in Porto Rico, and its growth into a School under the auspices of Columbia University, New York.

His later scientific work was concerned with sprue. His final conclusions, drawn from an examination of 4,000 cases, was that the great underlying condition was nutritional imbalance, and that when *Monilia* gains a footing in such cases it converts disordered nutrition into a definite morbid entity.

Part of the last paragraph of the book consists of these notable words. "The doctor's mission from this time forward, as I see it, is not so much a question of relief of pain, or of prevention of death, as it is a question of salvaging this man, this woman, this child for one hundred per cent. efficiency in the future. . . . This story tells how I have tried to do it."

Clayton Lane.

SCOTT (H. Harold) [M.D., F.R.C.P. (Lond.), D.P.H., D.T.M. & H., F.R.S.E.]. **Some Notable Epidemics.** With Preface by W. W. JAMESON, M.A., M.D., F.R.C.P.—pp. xix+272. With 1 fig. 1934. London: Edward Arnold & Co. [12s. 6d.]. [Review appears also in *Bulletin of Hygiene*.]

Few who are familiar with the names of the local epidemics of historical importance have easy access to the original reports. Yet it is impossible to obtain any idea from brief text-book references as to the kind of problems with which the investigators were faced or their method of approach to them. The original reports, too, dwell upon details which had to be considered in the light of the knowledge and prejudices of the time but which now seem largely irrelevant. They needed re-writing, sub-editing and commentary, and that is what the author of this book has done. Selection for publication from the substantial body of epidemics, about which official or other reports are in existence, must be arbitrary. Nineteen groups of local outbreaks, most of them single epidemics, have been chosen, all of them British, most occurring within the past half century and nearly all of special historical as well as epidemiological interest. Six were outbreaks of water-borne disease, including the famous Broad Street Pump epidemic of cholera and the classical Maidstone typhoid; ten were attributed to milk convection ranging from the sensational enteric outbreak of St. Marylebone in 1873 to the comparatively recent epidemic of sore-throat in 1929 at Brighton and Hove; one oyster-borne and the rest food-poisoning, dysentery or other alimentary infections carried by a variety of foodstuffs. The arrangement of the epidemics, partly chronological, partly in such a way as to illustrate the evolution of aetiological ideas and preventive practice, carries the reader from outbreak to outbreak with increasing interest. Each epidemic is discussed

in the light of modern knowledge and interspersed with illuminating, and sometimes humorous, comments which break the monotony of fact piled on fact in building up a hypothesis. A recent correspondent of the reviewer said about this book "The best detective yarns I have read for a long time." That is an interesting appreciation and indicates the writer's success in making the dry bones live, but the stories here retold are more than that, they show how repeated warnings to local authorities have been neglected until at last disaster fell upon them, how their niggardliness has cost them in the end more than they have saved, how careful epidemiological investigation can often arrive at true explanations without the aid of laboratory technique, and how the prevention of epidemics of alimentary disease depends on the careful application of sanitary principles all the time, for the infection is very often past before emergency measures can be put in force. Recent happenings in Malton and Denby Dale (water-borne typhoid), in Ogmore (water-borne dysentery), in Hertfordshire (milk-borne paratyphoid), in Chicago (amoebic dysentery) and in other places too numerous to mention show that complete security is still far from being attained. In tropical and other countries with relatively low hygienic standards, the risk is far greater. If war ever breaks out again over a wide area, recurrence of conditions favourable to outbreaks of intestinal infections is likely. Every public health official should be prepared to cope with epidemiological earthquakes of the kind depicted and brought together for his information in this book, and others will read it with profit and enjoyment.

R. M. F. Picken.

ROGERS (Leonard) [K.C.S.I., C.I.E., M.D., F.R.C.P., F.R.S.] & MEGAW (John W. D.) [K.C.I.E., B.A., M.B., Hon. D.Sc.] **Tropical Medicine.** Second Edition.—pp. xii+547. With 82 text figs. & 93 coloured figs. on 2 plates. 1935. London: J. & A. Churchill Ltd., 40 Gloucester Place, Portman Square. [15s.]

In the preface to this, the second edition of "Tropical Medicine," the authors again point out that "their aim from the onset has been to produce a handy inexpensive manual which would not compete with the larger works on tropical diseases." Their policy has been justified by the cordial reception awarded the first edition which appeared five years ago. The chief additions that have been made belong to the realms of the typhus fevers, yellow fever, malaria, leprosy and the nutritional diseases. The great feature of the book is that it is essentially *readable*, it deals with the subject matter from the point of view of the man *practising* medicine in the tropics, and contains the harvest of ripe experience gathered during many years.

It fell to the lot of the present writer to review the first edition and the invitation to offer criticisms and suggestions was taken advantage of. Some of the suggestions made have been adopted, others it is explained could not be. Others are now offered in the interest of all. The paragraph upon the immunizing mechanism in malaria is not clear. The authors note that the term bilious remittent malaria is falling out of use. Is it not time this division into clinical types, which savours of the middle ages, was replaced by a pathogenic explanation of the symptomatology? As it is, pathology is divorced from symptomatology and there is no obvious correlation. It is noted also in regard to malaria there is no mention of myocarditis. In the chapter dealing with tick relapsing fever there is no mention of ticks other than

O. moubata that transmit the infection and no mention of those cases which are resistant to treatment with arsenicals.

There is no mention of sprue as occurring in northern Europe. In reference to the chigger the statement is made "after all the eggs have escaped the insect is expelled and the small remaining ulcer heals. Any number, from one to hundreds, may be present; as a rule only a few are found at one time." It would be truer to say that the remains of the body of the chigger unless removed are eventually expelled by ulceration. In many cases the feet and hands may be literally honey-combed.

In regard to ankylostomiasis there is no mention in the text of the 50-100 per cent. incidence in Eastern Africa. Beriberi is not mentioned as occurring in Africa.

Although lathyrism is coupled with beriberi and pellagra as diseases associated with the use of a special article of diet and considerable space is given to the consideration of vitamins and their relation to deficiency diseases, no mention is made of MELLANBY's very interesting observations in regard to this disease.

Under yaws the causative organism is sometimes referred to as a spirochete elsewhere as a treponema. The disease in one place is said to be rarely inherited, in another place it is said to be not congenital.

These are given merely as examples of minor additions which might perhaps be added with advantage to the text. *H. S. Stannus.*

WU LIEN-TEH [Edited by]. **Manchurian Plague Prevention Service Memorial Volume 1912-1932.**—469 pp. With 2 text figs., 1 plan, 2 charts, 29 figs on 13 plates & 1 coloured plate. 1934. Shanghai: National Quarantine Service, 2 Peking Road.

This volume, which is dedicated to the delegates attending the 9th Congress of the Far Eastern Association of Tropical Medicine at Nanking in October, 1934, is as its title states a memorial volume. The Manchurian Plague Prevention Service, which the author has led with so much competence, has "passed into other hands." The two decades of useful work which the book commemorates have come to an end. We have here a collection of the best original articles that have appeared in the seven volumes of Reports of the Manchurian Plague Prevention Service. Of these, 16 concern plague, 4 cholera, 10 miscellaneous topics, and the appendix is a short autobiography of Dr. Wu. The plague articles making up as they do more than half the book will have a permanent value, especially those concerning the pneumonic form, for students of that disease. Attention is called to the list of wild rodents known or suspected to suffer from plague, revised to December 1932, and occupying, with the list of fleas, 14 pages.

Since Dr. Wu is only 55 years of age it is to be hoped that he may find a fresh field for his fruitful energies. *A. G. B.*

BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES
BULLETIN.

Vol. 32.]

1935.

[No. 3.]

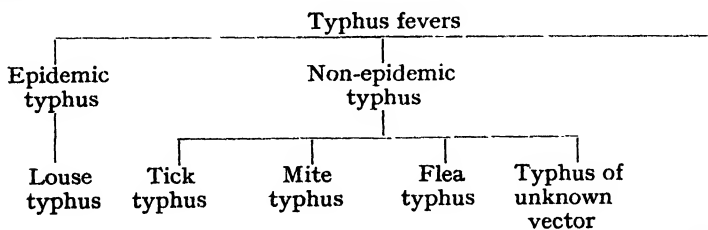
THE TYPHUS GROUP OF FEVERS.

MEGAW (John). **Typhus Fevers in the Tropics.**—*Brit. Med. J.* 1934. Aug. 11. pp. 244–246.

This paper was read in opening the discussion in the Section of Tropical Diseases at the Annual Meeting of the British Medical Association at Bournemouth in July 1934. It deals with typhus fever and especially the typhus fevers of the tropics from the historical, clinical and epidemiological points of view.

The author refers to his original observations in India in 1916 when he himself suffered from a definite attack of a typhus-like fever and was able to state that he had been bitten by a tick some 3 weeks before [see this *Bulletin*, Vol. 9, pp. 489–91]. In so far as this disease in India is concerned we are pretty much in the same position as we were some 20 years ago; that is to say similar cases are being described from time to time and in some it is stated "there was a clear history of tick bite," in others "no evidence could be obtained of the patient having been bitten by a tick." [It would be interesting if an investigation could be made in India on the lines of investigations made in America, France, South Africa and elsewhere which have shown that in similar diseases met with in these countries emulsions of infected ticks when inoculated into laboratory animals produce the disease.]

General Megaw suggests again that the simplest and most comprehensive classification of the typhus diseases is by means of the vector, as follows :—



D. Harvey.

OTTO (R.). Flecktyphus und endemische Fleckfieber. [**Epidemic or European Typhus and Endemic Typhus.**]—*Deut. Med. Woch.* 1934. Aug. 31 & Sept. 7 Vol. 60. Nos. 35 & 36. pp. 1299–1303; 1341–1344.

The first paper is a review of recent work on typhus fever dealing with the old world typhus and Brill's disease, Japanese River fever and

Rocky Mountain fever and tropical typhus. The subject of *Rickettsia* is also discussed and the various vectors—louse, rat, flea and mite. There is no new matter.

The second paper deals with immunity and serum reactions, especially the Weil-Felix reaction. Tables are given dealing with the diagnostic points between endemic and epidemic typhus and the question of the differentiation of the viruses is discussed. *D. H.*

ZINSSER (Hans). Sur la maladie de Brill et le réservoir interépidémique du typhus classique. [**Brill's Disease and the Interepidemic Reservoir of Classical Typhus.**—*Arch. Inst. Pasteur de Tunis.* 1934. July. Vol. 23. No. 2. pp. 149–154. [12 refs.]

The author discusses the question of the unity of the typhus viruses ; he is of opinion that the classical or human virus and the rat virus are two varieties of the same species which resemble one another in their antigenic properties but are not identical. He has studied two strains of the classical virus for several years but has never succeeded in transforming permanently the classical (human) virus into the rat virus.

A close study of 3 strains of virus obtained from 3 cases of Brill's disease has shown that all are of the classical or human type. It has also been shown that since 1910 some 500 cases of Brill's disease have occurred in New York and that 97·8 per cent. of these have been in Jewish immigrants from Europe and specially from Russia, Poland, and Rumania, centres of classical typhus in Europe. Brill's disease is therefore practically non-existent in people born in America and does not spread to them. In no instance was a second case noted in a family and there was no evidence of occupational infection. From these facts the author adduces that Brill's disease (classical virus) is not derived from a reservoir in the rat nor from any other source which could spread the disease to the local community from the immigrants.

The conclusion is that Brill's disease is classical typhus maintained in man, and that it is a recrudescence or relapse of a true typhus originally contracted in Europe.

Thus we have in America the two viruses of typhus. In the one man is the reservoir, in the other the rat. Brill's disease of New York and endemic typhus of the United States are two distinct entities. *D. H.*

PIJPER (Adrianus) & DAU (Helene). Die fleckfieberartigen Krankheiten des südlichen Afrika. [**The Typhus-like Diseases of South Africa.**—*Zent. f. Bakt.* I. Abt. Orig. 1934. Nov. 20. Vol. 133. No. 1/2. pp. 7–22. With 51 charts. [62 refs.]

This important paper gives full details of research work carried out in the laboratory of the senior author in Pretoria, South Africa.

There are three types or varieties of typhus-like disease in South Africa ; these resemble similar diseases described in other countries but are not identical. 1. Tick bite fever. 2. Epidemic typhus. 3. Sporadic typhus.

Tick Bite Fever.—This name was originally given by NUTTALL to the disease which was first described by SANT'ANNA in 1911. The disease is conveyed to man by larval ticks and the following have been shown

by the authors to be capable of transmitting the virus :—(a) *Amblyomma hebraeum*. (b) *Rhipicephalus appendiculatus*. (c) *Boophilus decoloratus*.

These small ticks climb on to the stalks of grass and attach themselves to man or animals ; they are veldt dwellers and are not found in houses or on domestic animals ; the reservoir of the disease is probably the small rodents of the veldt. In this respect the disease resembles Rocky Mountain fever and Indian tick typhus but differs from bouton-neuse fever. Injection of emulsion of these ticks produced the disease in man and animals and a rising titre of agglutination for Proteus X strains. Section of such ticks revealed the presence of Rickettsia in the malpighian tubules. In nature man is infected by the bite of the tick but infection may also be conveyed through the conjunctiva.

Two forms are met with, the mild or abortive form and the fully developed form. In the first the only symptom noted may be the presence of a primary sore at the site of the bite accompanied by a local lymphangitis. In the fully developed form the fever lasts for 8 to 10 days with primary sore, severe headache, appearance of a typical rash on the 5th day, stiffness of the neck and conjunctivitis. Typical temperature charts are shown. The primary sore is similar to that found in Japanese River fever and in bouton-neuse fever and when found is pathognomonic ; when the sore is situated between the toes or in a scrotal fold it may escape detection. This fully developed form of tick bite fever has previously been confused with typhus, meningitis, measles or typhoid fever.

Agglutination tests.—The sera of 85 cases of the disease were tested with the O variants of X19, X2 and XK, and tables are given in the text with detailed results of 28 of these ; the chief points noted are that there is a definite positive Weil-Felix reaction with rising titre of agglutination usually for all of the 3 variants of Proteus X employed. In some cases, but not in all, XK was agglutinated in higher titre than X19 but the serum of one and the same case may at one time agglutinate X19 in higher dilution and at a later date in convalescence XK, or conversely. On the whole, it is stated, the agglutination results are, in the sense of FELIX, in the nature of group reactions and the major antigen for this disease is still to seek. These remarks apply in considerable degree to the same reactions in the epidemic and sporadic types in South Africa.

Experiments with Guinea-pigs.—5 cc. of blood taken from patients on the first day of the disease was inoculated intraperitoneally into guinea-pigs and these animals reacted, after an incubation period of 5–6 days, with a very definite fever although they were not ill, did not lose weight and none died. The animals which had reacted to the virus did not react again when tested six weeks later although controls duly developed fever. The results of these experiments are clearly shown in numerous figures in the text. Animals which were killed during the fever showed enlargement of spleen and adrenals, hyperaemia of the brain, endothelial proliferation, and some slight swelling of the scrotum ; rickettsia were demonstrated from smears of the tissues. The virus was readily passaged through many generations in guinea-pigs, employing as a rule emulsion of brain as inoculum. The fever in guinea-pigs was further controlled by :—(a) Immunity tests ; (b) inoculation of emulsion of brain into rabbits with production of agglutinins in the serum ; (c) reinoculation of the virus from guinea-pig to man.

Mixture of immune serum with the virus prior to inoculation neutralized the virus; it was found that Rocky Mountain fever antiserum had no action on the virus of tick bite fever nor vice versa. Rabbits when inoculated with the virus developed agglutinins for all 3 variants, X19, X2 and XK.

Epidemic or Louse-borne Typhus.—The authors have studied the virus of this disease on the same lines. The results of the Weil-Felix reaction showed that the high titres for X19 met with in European cases are not found here; indeed the reaction, as already said, seems to be rather of the nature of a group reaction. Rabbits inoculated with this virus gave the same reaction as with tick bite fever virus; and the results of inoculation of the virus into guineapigs also varied somewhat from that usually obtained with the epidemic virus.

A sporadic type similar to endemic typhus described elsewhere is also met with in South Africa, but here also the results of the Weil-Felix reaction in patients' serum is similar to that obtained in cases of the epidemic type by the authors; XK may also be agglutinated. The virus both from cases of the disease and from rats caught in districts where cases had occurred was studied; this rat virus was similar to murine virus of Europe and America; no work so far has been done on rat fleas but it is probable that they carry the virus from rat to man.

Crossed immunity experiments were carried out with the viruses of the three types and gave the following results:—

1. Guineapigs immunized to the virus of tick bite fever are immune to the virus of epidemic typhus and sporadic typhus.

2. Guineapigs immunized to the virus of the local sporadic typhus are immune to the virus of tick bite fever but are *not* immune to the virus of epidemic typhus.

3. Guineapigs immune to the South African epidemic typhus virus are immune to the viruses of tick bite fever and sporadic typhus.

Tick bite fever closely resembles boutonneuse fever but differs in that it is carried by a field tick and not by a parasite of domestic animals (*R. sanguineus*). It is a much milder disease, yet the virus in the blood of patients is readily conveyed to animals, whereas the virus of boutonneuse fever is only conveyed with difficulty. A comparative table is given at the end of the paper.

D. H.

HENNESSEY (R. S. F.). **Typhus Fever in Uganda.**—*East African Med. J.* 1934. May. Vol. 11. No. 2. pp. 42–60. With 1 chart.

This disease was first noted in Kabale in the year 1932; the sera of patients gave a positive Weil-Felix reaction. Eighty-three cases in all have so far been reported; in one instance 36 out of 45 females in one dormitory at a mission station developed the disease. The mortality was nil. Investigation showed that the people were heavily infested with lice both of the head and body.

The author made a careful estimation of the Weil-Felix reaction using O variants of X19 and XK. Of 57 cases 28 gave a positive reaction with X19 and all were negative with XK; the interesting point is that although these were apparently cases of louse-borne typhus no serum gave a higher reading than 1/1,600.

Blood was taken from some of the patients and injected into guineapigs; these reacted with fever and also had some swelling of the scrotum. This was not marked externally but on examination gelatinous exudation was found and Rickettsia were demonstrated in the

fluid. Lice, collected from patients and also from people who had recently recovered from the fever, when emulsified and injected into guineapigs produced fever and infection of the scrotum; the brains of these guineapigs showed only slight evidence of the presence of the virus, more marked, however, than is usually the case with the virus of endemic typhus but less than one would expect to be produced by the virus of true typhus. D. H.

RAGIOT (Ch.) & DELBOVE (P.). Typhus endémique de Cochinchine. [**Endemic Typhus of Cochinchina: Pulmonary Symptoms.**]—*Bull. Soc. Méd.—Chirurg. Indochine.* 1934. Apr. Vol. 12. No. 4. pp. 449–453. With 1 chart.

—, DELBOVE (P.) & TRAN-VAN-TU. Typhus endémique probable de Cochinchine à Tan-an. Relations avec “l'épidémie de pneumococcies de l'Ouest Cochinchinois.”—*Ibid.* pp. 454–459.

A clinical description of cases of endemic typhus under the care of the authors.

These cases all gave a positive Weil-Felix reaction and the symptoms described are typical of the disease as met with in other parts of the world, except that in a number of cases very definite pulmonary symptoms were noted, ranging from slight bronchitis to broncho-pneumonia; many of these were fatal. These pulmonary symptoms masked the true nature of the disease which was, however, revealed by the rash and the positive Weil-Felix reaction. Louse-borne typhus is unknown in Cochinchina. D. H.

MESNARD (J.) & DELBOVE (P.). Existence, dans l'encéphale des rats de Saïgon, d'un virus rappelant le virus du typhus exanthématique. [**A Typhus-like Virus in the Brains of Rats of Saigon.**]—*Bull. Acad. Méd.* 1934. July 24. 98th Year. 3rd Ser. Vol. 112. No. 28. pp. 168–171.

In October 1933, 86 rats which were caught in Saigon, Cochinchina, were killed and emulsions of the brains inoculated into guineapigs. Three strains of virus were isolated; this virus gave in guineapigs the picture of a rat typhus virus, *i.e.*, fever, scrotal reaction and few brain lesions. The authors also noted that in infected guineapigs a rash appeared on the skin of the scrotum in male guineapigs and on the vulva of the female; this rash they consider to be diagnostic. Unfortunately owing to difficulty of transport of infected animals it was not possible to carry out crossed immunity experiments. Cases of endemic typhus fever had already been noted in the native hospital in the city of Saigon. D. H.

MOREIRA (João Affonso) & DE MAGALHÃES (Octavio). Typhus exantemático em Minas Gerais. [**Typhus Fever in Minas Gerais.**]—*Mem. Inst. Oswaldo Cruz.* 1934. Vol. 28. No. 2. pp. 225–234. With 7 graphs & 2 plates.

In a previous note the authors had stated that inoculation of 282 guineapigs with the virus of Minas Gerais typhus, killed 69·2 per cent. of the animals.

Since then with increase in the number inoculated, the fatality rate has considerably increased, so that amongst 692 animals inoculated, the rate was 90·6 per cent., which according to PARKER is the same as

that of guineapigs inoculated with the virus of Rocky Mountain spotted fever.

In the present paper the authors record a series of experiments on guineapigs bearing on the problem of crossed immunity in relation to the viruses of Minas Geraes, São Paulo typhus and Rocky Mountain spotted fever.

Their conclusions are as follows :—

1. Rocky Mountain spotted fever vaccine does not protect guineapigs against the virus of Minas Geraes typhus.

2. Guineapigs which have recovered from Minas Geraes typhus may be killed by inoculation with São Paulo typhus, or Rocky Mountain spotted fever.

3. Minas Geraes convalescent serum protects guineapigs when it is injected immediately after inoculation with the virus of São Paulo typhus, Rocky Mountain spotted fever, or Minas Geraes typhus.

J. D. Rolleston.

EPSTEIN (H.) & SILVERS (I. L.). Ueber den sogenannten endemischen Flecktyphus der Moskauer Ratten. [**The So-called Endemic Typhus of Moscow Rats.**]—*Giorn. d. Batter. e Immunol.* 1934. Apr. Vol. 12. No. 4. pp 593–612. With 2 figs. English summary (5 lines).

One hundred rats captured in Moscow were killed and emulsions from the brains of groups of six rats were inoculated into guineapigs; 32 per cent. of these developed fever.

The fever in the guineapigs is described in detail as regards incubation period, duration of fever, scrotal reaction and mortality. *Rickettsia* were demonstrated in the tunica.

Of 80 rats examined 37 per cent. gave a positive Weil-Felix reaction and 80 per cent. of the positive results in guineapigs were obtained from the rats with positive Weil-Felix reaction. It was also found that in guineapigs inoculated with the virus of epidemic (historical) typhus the Weil-Felix reaction was never positive, whereas in guineapigs inoculated with the rat typhus virus the Weil-Felix reaction which was negative in the normal animals became positive although not in any higher dilution of the serum than 1/40. As regards crossed immunity experiments with the various strains of virus it was found (1) that the strain of rat virus isolated by the authors protected one-half of the inoculated guineapigs against another Moscow strain; (2) that inoculation of guineapigs with the human typhus virus protected 30 per cent. of the guineapigs against the rat strain; (3) the rat strain of typhus virus did not protect guineapigs against the human typhus virus.

An interesting point was that guineapigs infected by means of an emulsion of fleas fed on infected rats were found to be protected against the local strain of human typhus virus.

D. H.

NICOLLE (Charles) & SPARROW (Hélène). Etude d'un virus typhique murin, isolé des rats du port de Tunis. [**Study of a Typhus Virus Isolated from Rats in the Port of Tunis.**]—*Arch. Inst. Pasteur de Tunis.* 1934. Aug. Vol. 23. No. 3. pp. 247–303. With 9 charts. [Summary appears also in *Bulletin of Hygiene.*]

A Weil-Felix reaction carried out on the sera of 880 rats in the Port of Tunis was positive in a titre of 1/80 or over in 4.4 per cent., and in a titre of 1/40 or over in 9.9 per cent.

Weigl's method of using for agglutination a *Rickettsia* suspension from the intestines of lice, instead of *Proteus X19*, was found to be very satisfactory. The test seemed to be slightly more sensitive, and the titre against a Mexican (rat) virus was sometimes rather higher than against the classical European virus, thus giving a clue to the probable nature of the infecting agent.

Two strains of virus were isolated from rats and studied carefully. They were similar to murine viruses described in other parts of the world. They caused fever and orchitis in guineapigs. In rats they gave rise to a fever of short duration, and led in about one-third of these animals to the development of a positive Weil-Felix reaction. Their pathogenicity to man appeared to be relatively feeble, and persons who contracted infection in the laboratory suffered only mild attacks of typhus.

G. S. Wilson.

S. AVOOR (Sadashivarao R.) & VELASCO (Roberto). **The Survival of Varieties of Typhus Virus in Mouse Passage, with Particular Reference to the Virus of Brill's Disease.**—*Jl. Experim. Med.* 1934. Sept. 1. Vol. 60. No. 3. pp. 317–322. With 1 chart.

Three different viruses were employed in this research :—

1. A Mexican murine virus.
2. A true typhus virus obtained from Europe.
3. A virus obtained from a case of Brill's disease in Boston, U.S.A.

Virus No. 1 gave the usual reactions of a murine or endemic typhus virus in guineapigs and rats. Nos. 2 and 3 gave the reactions of the human or old world historic virus in the same animals. The 3 viruses were tested by inoculation into mice and the results of the experiments show that the European typhus virus cannot be maintained for more than two generations in mice by brain peritoneum passage, whereas the murine Mexican variety can be carried on by this method in mice for at least eleven generations. The virus of Brill's disease from three different sources behaved like the European virus, an observation which strengthens the opinion expressed by ZINSSER that Brill's disease represents an imported strain of the classical European infection. [If it is generally accepted that Brill's disease as it occurs in New York and Boston is due to the European virus (historic or human type) and, as suggested by ZINSSER, is not carried by the rat flea or the louse, it would be necessary to distinguish between Brill's disease and endemic typhus, the latter term being reserved for the typhus-like disease which occurs in America, in Mexico, in Europe and in other parts of the world and is caused by the murine virus and is carried from the rat to man by the rat flea.]

D. H.

MONTEIRO (J. Lemos). Etude comparative entre le "typhus exanthématique de Sao Paulo" (rickettsiose néotropical) et le typhus exanthématique Chili (rickettsiose épidémique) par l'épreuve de protection avec des sérums de convalescents. [**Comparative Study of the Virus of São Paulo Typhus (R.M.F.) and Epidemic Typhus of Chile.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. pp. 1131–1132.

Five sera from cases of epidemic typhus in Chile were tested for action on the virus of São Paulo fever. They were mixed with varying quantities of virus and injected into guineapigs; no protective action whatever was noted.

This negative result shows that the typhus of Chile is a true typhus and not allied to Rocky Mountain fever.

D. H.

LÉPINE (P.). Neurotropisme et adaptation du virus murin du typhus exanthématique. [**Neurotropism and the Adaptation of the Murine Virus of Typhus.**]—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 536-540.

The author has noted in his investigation of rat typhus viruses in the Mediterranean area that these vary in virulence for guineapigs and rats. Strains of virus which have at first produced fever and marked scrotal reaction and no brain lesions, may, when they lose virulence, cease to produce orchitis but produce marked brain lesions, *i.e.*, they become neurotropic. Strains isolated from wild rats during non-epidemic periods are of this latter type, they resemble the true or historic typhus virus in their action on experimental animals. During epidemic periods the virus isolated from rats is virulent for guineapigs and produces orchitis.

The author suggests that in non-epidemic periods the virus shelters in the brains of rats. He also suggests that a like change in the rat virus may take place when it is taken up by the louse and passed from man to man, *i.e.*, the endemic virus is transformed into the epidemic, the "rat" virus into the "historic."

D. H.

RONSE (Marguerite). Adaptation du virus du typhus murin aux mulots et aux pigeons. [**Adaptation of the Virus of Rat Typhus to Field Mice and Pigeons.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 19. pp. 358-360.

Field mice were inoculated with the virus and later guineapigs were injected from them. Pigeons were also shown to be susceptible.

D. H.

DYER (R. E.). **Endemic Typhus Fever. Susceptibility of Woodchucks, House Mice, Meadow Mice, and White-footed Mice.**—*Public Health Rep.* 1934. June 22. Vol. 49. No. 25 pp. 723-724.

Woodchucks (marmots), house mice, meadow mice and white footed mice were all found to be susceptible to the virus of endemic typhus fever.

D. H.

VARELA (Gerardo) & GAY (M. A. Parada). Production d'orchite au moyen de la souche tunisienne de typhus épidémique. [**Orchitis produced by a Tunis Strain of Epidemic Typhus.**]—*C. R. Soc. Biol.* 1934. Vol. 116. No. 23. pp. 731-732.

Professor NICOLLE had supplied the authors in Mexico with a strain of typhus virus (old world) from Tunis. By employing a special method, inoculation of the virus intraperitoneally into rats followed by daily inoculations of fresh guineapig blood and then inoculation of the washings of the peritoneum of these rats into guineapigs, the virus after 12 passages lost its original characters and gave the reactions of a rat typhus virus, *i.e.*, scrotal reaction in guineapigs and fever in rats. This virus retained these characters for a further 12 passages without inoculations of fresh blood.

The authors claim that they have demonstrated that the historic typhus virus can be changed into a rat typhus virus, the non-orchitic into the orchitic.

D. H.

JELIN (W.), LINETZKAJA (A.) & GROSSMANN (J.). Die Bedeutung des retikuloendothelialen Systems bei Fleckfieber. [**The Rôle of the Reticulo-Endothelial System in Typhus Fever.**]*—Arch. f. Schiffshygiene.* 1934. May. Vol. 38. No. 5. pp. 202–206. With 6 figs.

The authors refer to previous work on the same lines in bacterial and protozoal diseases; they find that if the spleen is removed and the remainder of the reticulo-endothelial system blocked by means of India ink rabbits develop a marked febrile reaction when inoculated with typhus virus and also lesions are found in the brain and internal organs; whereas only inapparent infection occurs in rabbits not so treated. Guinea-pigs treated in the same way develop a much more severe illness than is shown in untreated animals. The R.E.S. therefore plays a prominent part in the mechanism of infection and immunity in typhus fever.

D. H.

RONSE (Marguerite). Infection exanthématique par voie digestive. [**Typhus contracted by the Digestive Tract.**]*—C. R. Soc. Biol.* 1934. Vol. 116. No. 19. pp. 360–363.

The author repeated the work of NICOLLE with typhus virus and has shown that rats, voles, dwarf mice, rabbits and hedgehogs can be infected by the digestive route.

Bread was soaked in emulsion of the brain of infected guinea-pigs and the animals were fed on this. Infection was proved by injection of the brain of the experimental animals into normal guinea-pigs which reacted with fever and swelling of the scrotum. No fever was noted in the rats, which had an "inapparent infection."

D. H.

EPSTEIN (H.), TUREWITSCH (E. I.) & EXEMPLARSKAJA (E. W.). Zur Mikroskopie des Flecktyphus. [**Microscopic Appearances in Typhus.**]*—Giorn. Batter. e Immunol.* 1934. Apr. Vol. 12. No. 4. pp. 659–667. English summary (2 lines).

Demonstration of Rickettsia bodies in the cells of the blood of typhus patients.

By special differential staining methods and examination by means of dark ground illumination the authors claim that they can demonstrate Rickettsia bodies in monocytes in the blood of typhus patients and that they can distinguish these from normal granules in the cells; they consider that these bodies are identical with Rickettsia bodies seen in the endothelial cells of the tunica of infected guinea-pigs and in the cells of the intestines of lice.

D. H.

LÉPINE (P.) & BILFINGER (F.). *Rickettsia* et typhus exanthématique. [**Rickettsia and Typhus.**]*—Bull. Soc. Path. Exot.* 1934. Apr. 11. Vol. 27. No. 4. pp. 298–304.

The authors have repeated their investigations on the filterability of the virus of typhus. They find that this virus does *not* pass through

filter candle L3, contrary to what has been recently stated by PANAYOTATOU [this *Bulletin*, Vol. 31, p. 245]; the same investigator has also stated that *Rickettsia* can be readily demonstrated in smears from the spleen of infected guineapigs; this is contrary to the experience of the authors who found that although emulsions of spleen from infected guineapigs were highly infective no *Rickettsia* could be found in smears made from the spleen, an interesting observation and one which points to an ultra microscopical form of the *Rickettsia*. In rats dead of typhus infection numerous *Rickettsia*, readily stained, appear in the peritoneal cavity; these bodies rapidly disappear and cease to take the stain yet the fluid retains its virulence. In the spermophile an animal readily infected and the tissues of which are highly infective, *Rickettsia* are rarely seen in the glands or tissues; also the tissues (brain and spleen) of guineapigs are infective before *Rickettsia* appear in the peritoneum or scrotum. In spite of these findings the authors are convinced that *Rickettsia* and the virus of typhus are one and the same but there is much yet to be explained. Certain cells are found in the spleen of infected animals which show numerous granular inclusions which stain in the manner of *Rickettsia* but are *not* included *Rickettsia*; these cells have not been noted in control animals. It is suggested that there are two forms of *Rickettsia*, the ordinary bacillary form and the granular intracellular form.

D. H.

ZIA (Samuel). **The Cultivation of Mexican and European Typhus *Rickettsiae* in the Chorio-Allantoic Membrane of the Chick Embryo.**—*Amer. Jl. Path.* 1934. Mar. Vol. 10. No. 2. pp. 211-218. With 3 figs. on 1 plate.

Emulsion of tunica from guineapigs infected with typhus virus was dropped on to the exposed membrane of eggs containing live chick embryos, these were incubated and a reaction resulted; material from the thickened membrane produced infection when injected into guineapigs; also *Rickettsia* could be demonstrated in smears made from the thickened membranes. Similar results were obtained with Mexican and European typhus virus. Some figures are given showing the histological changes produced by the virus in the membranes of the chick embryo.

D. H.

- i. NISHIBE (Masujiro) & MIYAZAWA (Masaei). **On the Growth Inhibiting Action of Immune Tissues and Plasma on *Rickettsia orientalis*. A Study with Tissue Cultures.**—*Trans. Soc. Path. Japon.* 1933. Vol. 23. pp. 747-750.
- ii. YOSHIDA (S.) & UEDA (M.). **Tissue Culture of the So-called Manchurian Typhus Fever Virus. Part I. The Relation of Virulence and *Rickettsia* according to the Kinds of Cultured Tissues.**—*Ibid.* pp. 753-754.

i. The cultures were inoculated with rabbit testicle cells containing *R. orientalis* and (1) normal tissue, *i.e.*, rabbit testicle, (2) testicle of immune rabbits, (3) immune plasma.

It was found that the multiplication of the *Rickettsia* was marked in the tubes to which normal tissue had been added, much less in the tubes with immune plasma and hardly any in the tubes to which immune tissue had been added

ii. The medium employed was heparin plasma with infected tissue cells and normal tissue. Omentum, lung, spleen, marrow, etc., were employed as the normal tissue and it was found that omentum gave much the best results; that is, the multiplication of *Rickettsia* was greatest in the tubes with omental cells. *D. H.*

KLIGLER (I. J.) & ASCHNER (M.). **Immunization of Guinea Pigs with Formalized Cultures of European Strain of Typhus Rickettsia.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Apr. Vol. 31. No. 7. pp. 808–809.

The authors have recently shown that it is possible to cultivate *Rickettsia in vitro*. Guinea pigs have now been successfully immunized with formalized suspension of fresh virulent culture as well as with older cultures which were no longer infective for guinea pigs. Ten days after the last injection of the vaccine the guinea pigs received a test dose of 80 infective doses of brain virus and 16 days later 800 doses were given without any reaction; all non-vaccinated controls reacted. *D. H.*

BLANC (Georges), NOURY (M.), BALTAZARD (M.), BRUNEAU (J.) & BARNEAUD (J.). Nouvelles expériences de vaccination humaine contre le typhus exanthématique par vaccin vivant. Infection et immunité. [**Vaccination of Man against Typhus with Living Vaccine.**]—*Bull. Acad. Méd.* 1934. May 1. 98th Year. 3rd Ser. Vol. 111. No. 16. pp. 582–592. With 6 figs.

This living vaccine is prepared by emulsifying material from the spleen and tunica of guinea pigs infected with a mild strain of endemic typhus; it has been proved that passage of this mild virus through a series of animals does not increase the virulence. The emulsion of the virus in normal saline is treated by contact with ox bile for two hours; the vaccine is diluted 1,000 times and inoculated in doses of 2 cc.

The authors are of opinion that it is not possible to vaccinate against typhus without causing an infection; inoculation with the living bile-treated vaccine causes an inapparent infection with subsequent immunity. 1,000 people can be vaccinated with the material obtained from an infected guinea pig. *D. H.*

SUZUKI (K.). Untersuchung ueber *Rickettsia*-Infektion (sogenanntes Rattenfleckfieber-Virus) und Weil-Felix-Reaktion bei Ratten in Hamburg. [**Research on Rickettsia Infection (So-called Rat Typhus Virus) and the Weil-Felix Reaction in Rats in Hamburg.**]—*Taiwan-Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. Apr. Vol. 33. No. 4 (349). [In Japanese. German summary pp. 58–76. With 25 figs. [21 refs.]]

The author refers fully to recent work on the same lines in America and in Europe. The sera of ten rats (1 ship rat and 9 decumanus) were tested; 1 agglutinated OX19 in a dilution of 1 in 50 and 4 agglutinated X19 (*sic*) in 1–200. Emulsions of the brains of the rats were injected intraperitoneally into male guinea pigs; in 3 instances positive results were obtained, *i.e.*, fever and orchitis; these strains were passaged in guinea pigs and numerous temperature charts are given in the text along with photographs of the scrotal condition showing rickettsia in the cells of the tunica. These rickettsia were not observed in the guinea pigs directly inoculated from the rats but appeared about the

3rd or 4th passage. It is also stated that a positive Weil-Felix reaction up to a dilution of 1/200 was obtained in the infected guineapigs. [See papers by DURAND.] D. H.

LAIGRET (Jean) & DURAND (Roger). Sur les caractères antigéniques d'une souche tunisienne de *B. proteus*. [**Antigenic Characters of a Tunis Strain of Proteus.**]*—C. R. Soc. Biol.* 1934. Vol. 116. No. 17. pp. 119–120.

This strain of *Proteus* (S24) was isolated from the blood of a mouse which had died of an infection with the bacillus. The O form of S24 was readily agglutinated by the serum of cases of typhus fever to the same titre as OX19; S24 is apparently identical with that classical strain except that when OS24 is inoculated into rabbits their serum agglutinates S24 and X19 and also XK; whereas X19 does not produce agglutinins for XK. S24 resembles the strain of *Proteus* recently isolated in Lima and associated with the São Paulo type of Rocky Mountain fever which also produces agglutinins for XK when inoculated into rabbits. D. H.

DURAND (Roger). Réaction de Weil et Félix positive chez le cobaye typhique. [**Positive Weil-Felix Reaction in Guinea-pigs with Typhus.**]*—C. R. Soc. Biol.* 1934. Vol. 116. No. 17. pp. 118–119.

In man and in rabbits a positive Weil-Felix reaction has been noted but so far although guineapigs react to the virus the serum does not give a positive reaction.

The authors have, however, shown that if the virus (emulsion of brain of infected guineapig) is inoculated directly into the heart of the guineapig a positive reaction is obtained although only in low titre 1/50. If the animal is at the same time inoculated intraperitoneally with starch (tapioca) a slightly higher titre can be obtained, 1/100.

D. H.

DURAND (Roger). Agglutination du proteus dans le typhus exanthématique du cobaye. [**Proteus Agglutination in Typhus of Guinea-pigs.**]*—Arch. Inst. Pasteur de Tunis.* 1934. July. Vol. 23. No. 2. pp. 155–237. With 1 chart. [71 refs.]

This is a record of a most careful research on the question of the Weil-Felix reaction in guineapigs. The first part of the paper deals with the Weil-Felix reaction in general and the necessity of utilizing only O emulsions of *Proteus*.

Practically all cases of true typhus give a positive Weil-Felix reaction as do also monkeys, rabbits and rats when inoculated with the virus or in the case of the last when infected in nature; but although guineapigs are the animals most commonly employed and most useful in experimental work on typhus their serum does not agglutinate *Proteus* X19 or any of the other strains of *Proteus* utilized in typhus work; yet when the virus of typhus is inoculated into guineapigs they develop a marked fever which is followed by immunity but not by production of agglutinins for *Proteus*. Also, if the animals are inoculated with cultures of *Proteus* they develop agglutinins for that bacillus just as readily as do rabbits or rats. It was noted that if guineapigs which have recovered from an attack of experimental typhus are inoculated with living emulsions of *Proteus* they produce agglutinins for the homologous

bacillus but not to such a high titre as do guineapigs which have not previously been infected with typhus virus; on the other hand in guineapigs which have been inoculated with *Proteus* and are subsequently infected with typhus virus the agglutinins for *Proteus* are in no way affected.

The sera of typhus guineapigs was also tested for other reactions besides agglutination but neither flocculation, precipitation nor complement fixation was detected; neither could any agglutinins for *Br. abortus* or allied bacteria be found.

It might be thought that there was an inhibitory substance for typhus agglutinins in the sera of guineapigs but the authors state that this is not the case; several reasons for this opinion are given:—

1. *Proteus* X19 treated by the serum of guineapigs retains its agglutinability by other typhus sera.

2. Guineapig serum does not remove or reduce the agglutinins from other typhus sera, man or rabbit. In addition to the serum of typhus guineapigs the whole blood, plasma and spleen pulp also give negative results when tested for the Weil-Felix reaction. Different methods of inoculating the virus into the animals were tried to ascertain whether a positive Weil-Felix reaction could be obtained; intracerebral and intraperitoneal inoculation of the virus were both followed by negative results but when the virus was inoculated directly into the heart there was evidence of some slight but quite distinct agglutination of *Proteus* X19 after the fever but not in higher titre than 1/25.

Finally after trying out various methods without success it was found that if the animals are cholesterized so that the cholesterol content of the blood is high and if powdered tapioca is introduced into the peritoneum and the virus is then inoculated intracardially a positive Weil-Felix reaction is produced in the sera of the guineapigs. D. H.

i. DE ASSIS (Arlindo). Estudos sobre “*Proteus* XL.” I. Analyse agglutinante. [**Agglutination Reactions of *Proteus* XL.**].—*Brasil-Médico*. 1934. Apr. 14. Vol. 48. No. 15. pp. 253–256. English summary.

ii. —. II. Agglutinabilidade em séros humanos.—*Ibid.* No. 16. pp. 274–275. English summary.

- i. The sera of rabbits immunized with OXL (Lima São Paulo strain) develop agglutinins for OXL and OX19; indeed OX19 may be agglutinated in higher titre than OXL. Group agglutinins for OX2 and O *Proteus Americanus* (OXA) were also noted but no agglutinins for OXK were produced.

- ii. From agglutination tests on 270 human sera taken from cases of fever such as typhoid, tubercle, malaria, and syphilis, slight non-specific agglutination of the O variant of *Proteus* OXL (strain of Lima, São Paulo) was noted. This non-specific agglutination of OXL was quite distinct from the true Weil-Felix reaction. In this respect OXL and OX19 differ from OXK. D. H.

DINGER (J. E.). Infecties met proteus van het type Kingsbury. [**Infections with *Proteus*, Type Kingsbury.**].—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. May 22. Vol. 74. No. 11. pp. 661–672. English summary.

Two cases of infection of the bladder are described in which cultures of proteus organisms were obtained. These strains were proved to be

culturally identical and serologically similar to the Kingsbury strain XK. One strain showed relationship both with the O and H antigen; the other differed in the H antigen and was only partially related in the O. In both cases the patients' sera contained agglutinins for OXK. In neither was there any symptom of typhus fever. D. H.

DE ASSIS (Arlindo). Estudos sobre *Proteus americanus*, Pacheco (Proteus XA). I. Agglutinabilidade da variante OXA nas rickettsioses humanas. [Studies on *P. americanus* (XA).]—*Brasil-Medico*. 1934. July 14. Vol. 48. No. 28. pp. 552-554. English summary.

The sera of 6 patients suffering from typhus fever of São Paulo and of 3 convalescents from true or epidemic typhus of the Argentine were tested for agglutinins against emulsions of *Proteus americanus* OXA and also OX19, OX2, OXL and OXK. The results reveal a close relationship between OXA and OXK the Kingsbury strain. D. H.

DE ASSIS (Arlindo). Estudo sobre *Proteus americanus* Pacheco (Proteus XA) II. Estudo geral do agglutinogenio flagellar (HO). [*Proteus americanus* (Proteus XA): its H Agglutinins.]—*Brasil-Medico*. 1934. Aug. 11. Vol. 48. No. 32. pp. 635-639. English summary.

The author cultivated the organism for six months on agar and found that this species exhibited a tendency to revert to the O type of agglutinin. The sera of rabbits immunized with living cultures proved to contain also group agglutinins for HXK, and vice versa, sera of animals immunized with HXK cultures contained group agglutinins for Proteus XA. Absorption tests showed that the flagellar agglutinins for each were quite distinct, those of Proteus XA "seemed definitely more complex." Proteus XA sera did not agglutinate flagella variants of Proteus X19, X2 and XL. A so-called *Pr. mirabilis* N.2 strain had flagellar agglutinogens identical with those of *Pr. americanus*, and this (*Pr. mirabilis* N.2) has been isolated from the nasal discharges of a man who had never suffered from any disease resembling typhus, and *Pr. americanus* has also been isolated from the blood of a man with an infection apparently having no connexion with any known Rickettsia disease. H. H. S.

KYU (U. F.). Clinical Observations on the So-called Two-Weeks Fever (or Sporadic Eruptive Fever) in Formosa.—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1934. May. Vol. 33. No. 5 (350). [In Japanese. pp. 832-852. With 5 charts [25 refs.] English summary pp. 88-89.]

KOJIMA (T.), YAMANAKA (S.) & KYU (U. F.). Studies on the So-called Two-Weeks Fever (or Sporadic Eruptive Fever) in Formosa.—*Ibid.* [In Japanese pp. 853-872. With 5 figs. (4 coloured) on 1 plate. [21 refs.] English summary pp. 89-96.]

For many years a disease known locally as "two weeks fever" has been known to occur in Formosa. It is a typhus-like disease of mild form and the serum of patients gives a positive Weil-Felix reaction. The authors have isolated a virus from cases which in its effects on

guineapigs resembles the virus of rat typhus ; Rickettsia were readily found in the lesions in the scrotum. It has also been possible to test the local virus against a virus of true typhus and crossed immunity has been demonstrated.

A similar virus has also been isolated from rat fleas caught on rats on premises where cases of the two weeks fever had occurred. *D. H.*

CUMMING (James G.). **Rocky Mountain Spotted Fever invades the East.**—*Southern Med. Jl.* 1934. Sept. Vol. 27. No. 9. pp. 783-788. With 5 figs. (1 map).

MILAM (D. F.). **Rocky Mountain Spotted Fever in North Carolina.**—*Ibid.* pp. 788-792.

These two papers deal with Rocky Mountain fever as it occurs in the Central and Eastern sections of the United States, especially in N. and S. Carolina. A full clinical description of the disease is given with excellent photographs showing the appearance of the rash.

As regards prevention it is pointed out that although destruction of small rodents and keeping of fowls around homesteads may aid in the reduction of ticks, yet the best method is by means of the vaccine prepared from infected ticks.

The tick which causes the disease in man in the Eastern States is the common dog tick of America, *Dermacentor variabilis*. This tick in the larval form feeds on small rodents, squirrels, field mice, rabbits, etc., and in the adult form on dogs and occasionally on man. A warning is given of the danger involved in removing ticks from dogs and crushing them in the fingers since infection has been carried in this way in Rocky Mountain fever and boutonneuse fever. *D. H.*

MILAM (D. F.). **Rocky Mountain Spotted Fever in North Carolina.**—Reprinted from *Southern Med. & Surgery*. 1933. Sept. Vol. 95. No. 9. 4 pp. & 1934. Feb. Vol. 96. No. 2. 2 pp.

In 1933 18 cases of Rocky Mountain fever were reported in North Carolina ; previously only one case had been recognized, probably cases had been diagnosed as " typhus fever."

In the present series it was noted that the rash covered the entire body including the palms and soles.

Source of infection.—Small wild rodents are the reservoir of the virus and ticks as larvae and nymphs feed on these and become infected ; the adult ticks, still infective, feed for preference on the dog, the horse and man ; these adult ticks lay eggs in which the infection is maintained. The tick season is the fever season.

A table is shown giving the chief differential points between Rocky Mountain fever and endemic typhus.

Rocky Mountain Fever.

Endemic Typhus.

Epidemiology.

- | | |
|--|------------------------------|
| 1. Rural | Urban. |
| 2. History of tick bite in 75 per cent. of cases | Premises infested with rats. |
| 3. More children attacked. | Adults, middle age. |
| 4. One or two cases in same family. | Sporadic. |

*Rocky Mountain Fever.**Endemic Typhus.**Clinical.*

- | | |
|---|---|
| 1. Onset sudden. | Onset sudden. |
| 2. Fever up to 107° lasts about 3 weeks, lysis. | Fever lower, crisis end of 2nd week. |
| 3. Rash first on wrists and ankles then general, including palms and soles. | First on trunk, flexor surface of limbs, rarely on face or palms and soles. |
| 4. Pulse rate higher. | Pulse rate lower. |
| 5. Fatality 25 per cent. in eastern type | Under 5 per cent. |

Thirty-seven cases noted in 1934 varied from very mild to severe and fatal. Inoculation of blood taken from one of these mild cases gave a positive reaction in a guineapig.

The local medical men are of opinion that this is no new disease in the district but that similar cases have been met with for 20 years and diagnosed as typhus. There is, however, probably an increase in the number of cases as well as in that of endemic typhus. *D. H.*

GIMBERT, ANDREOLI, HOUSSIAUX & FOUREST. Fièvre boutonneuse grave. Début conjonctival. Forme délirante ataxodynamique. Absès de fixation. Sérum de convalescent. Guérison. [**Severe Form of Boutonneuse Fever of Conjunctival Onset.**].—*Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1934. May 14. 3rd Ser. 50th Year. No. 15. pp. 614-615.

A very severe case of boutonneuse fever, the initial lesion being in the conjunctiva. The nervous symptoms were particularly alarming. Two doses of convalescent serum were given, followed by recovery. *D. H.*

RAYBAUD (A.). Comment l'appellerons-nous : fièvre boutonneuse, exanthématique, dothiendermie ? [**Nomenclature of Marseilles Fever.**].—*Marseille-Méd.* 1934. June 5. Vol. 71. No. 16. pp. 693-695.

In an article in the *Lyon-Médical* of May 1934, CHALIER, PLAUCHU & BADINAND have proposed that the disease at one time known as exanthematous fever of Marseilles should now be called "dothiendermie aiguë." Raybaud points out that after a full discussion by a Commission of the International Congress of Hygiene of the Mediterranean it was decided that this disease should be known as "boutonneuse" fever, the name originally given to it by CONOR and BRUCH in Africa in 1910. Raybaud therefore deprecates the proposal to give still another name, one which, as he points out, has no advantages other than its derivation from the Greek. *D. H.*

PIJPER (Adrianus). **Tick-Bite Fever. A Clinical Lecture.**—*South African Med. J.* 1934. Aug. 11. Vol. 8. No. 15. pp. 551-556.

This paper is a clinical lecture on and demonstration of a typical case of "tick bite fever." The author prefers to retain the name of "tick bite fever" originally given to the disease by NUTTALL, although he agrees that it may give rise to confusion with "tick fever," i.e., relapsing fever carried by ticks.

The present case showed a very definite primary sore similar to the "tache noire" of boutonneuse fever, which disease tick bite fever resembles in many respects although they are not identical.

The disease in South Africa is a mild one with fever lasting ten days and severe headache and a rash of maculae or maculopapules; but it may occur in "forme fruste" with primary sore and inflamed lymphatics without fever. The Weil-Felix reaction is positive but may only appear after the fever is over. *D. H.*

LENTJES (L. J. M.). Een geval van tropisch ("shop") typhus met primair affect. [**Tropical ("Shop") Typhus with a Primary Lesion.**—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. July 3. Vol. 74. No. 14. pp. 876-879.

"Scrub" typhus and mite fever give a serum reaction of agglutination with the Kingsbury strain of *Proteus*, while "shop" typhus serum agglutinates *Proteus* OX₁₉. Again, mite fever exhibits a primary lesion while "scrub" typhus does not, nor has any such primary lesion been described in "shop" typhus. The interest of the present case lies in the fact that it was a typical case of typhus fever, the serum agglutinated *Proteus* OX₁₉ and was negative to the Kingsbury strain, and there was a well marked primary lesion. The conclusion is therefore reached that "shop" typhus may have a primary lesion as illustrated by this unique case, but that in all probability it is usually evanescent.

On the day that the patient fell ill he noticed a small round swelling on the scrotum which was oozing a little and was itchy and burning. On admission to hospital there was found an ulcer, 7 by 5 mm., with a sharp pale margin, small surrounding red halo and dirty yellow-grey base on the middle of the scrotum just under the root of the penis. There was no induration and the regional lymph nodes were moderately swollen. This was the primary lesion. No history was forthcoming of its origin. Trauma and venereal infection were excluded.

W. F. Harvey.

HAYASHI (Naosuke), MATSUOKA (Shigeji), KATO (Taro) & OKAMOTO (Niichizo). **Studies on Tsutsugamushi Disease. Report for 1932.**—*Trans. Soc. Path. Japon.* 1933. Vol. 23. pp. 735-738. With 1 coloured fig.

The morphology of R. tsutsugamushi.—Exceedingly minute forms have been noted 0.2 to 0.25 μ in diameter. In the opinion of the author these are the "initial forms"; they increase in size and finally divide.

Etiology.—*R. tsutsugamushi* has been demonstrated in the spleens of wild rats caught in areas where the disease is epidemic. The same condition has been noted in the case of guinea-pigs placed in infected areas of the country and bitten by mites.

Prevention.—Vaccination by means of injection of infected tissues has been employed. *D. H.*

Kō (Tōuu). Klinische Beobachtungen in 100 Fällen von Tsutsugamushi-Krankheit. [**Clinical Observations on 100 Cases of Tsutsugamushi Disease.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. Apr. Vol. 33. No. 4 (349). [In Japanese. German summary p. 51.]

During the 20 years 1911-1931 the author has had under his care 100 cases of this disease.

The cases occurred every year in the summer season among field workers and their families, the ages of the patients varying from 1 year to 76 years. The fatality rate was about 20 per cent. *D. H.*

CHIANESE (Raffaele). Due casi di febbre esantematica estiva del Litorale Mediterraneo.—*Terapia*. 1934. Apr. Vol. 24. No. 178. pp. 109-116. [27 refs.]

DOPFF (C. Soler) & CONFORTO (A. Valls). Observaciones locales de fiebre exantemática mediterránea.—*Rev. Méd. Barcelona*. 1934. Oct. Year 11. Vol. 22. No. 130. pp. 289-294. With 2 charts & 2 figs. on 1 coloured plate.

FUNK (William H.). A Case of Endemic Typhus or Brill's Disease in the Philippine Islands.—*U.S. Nav. Med. Bull.* 1934. Oct. Vol. 32. No. 4. pp. 517-518.

DENGUE AND SANDFLY FEVER.

HOFFMANN (J. M.), MERTENS (W. K.) & SNIJDERS (E. P.) **The Transport of the Javanese "Endemic Dengue" to Amsterdam.**—Reprinted from *Proc. Acad. Sci. Amst.* 1932. Vol. 35. No. 6. pp. 909-910.

Blood was taken from dengue patients in Java on the second day of the disease. The serum was dried, placed in a refrigerator and brought to Amsterdam. The dried serum was redissolved and inoculated into volunteers 285 days after it had been taken in Java; one of these volunteers developed a typical attack of dengue and the disease was passed to other volunteers. It is now proposed to compare the virus from Java with that already obtained from Sumatra [see this *Bulletin*, Vol. 28, p. 619]. *D. Harvey.*

JESIORAN (R.). *La dengue dans le bassin méditerranéen.* [**Dengue in the Mediterranean Basin.**] [Thesis: University of Algiers.]—116 pp. [16 pages of refs.] 1933.

In this comprehensive and detailed review of the subject of dengue in Southern Europe over 200 papers on the subject have been consulted, most of which have already been summarized in this *Bulletin*.

D. H.

GRIZAUD (H.). *Au sujet de quelques cas de "fièvre rouge" à la Guadeloupe.* [**"Fièvre rouge" in Guadeloupe.**]—*Bull. Soc. Path. Exot.* 1934. May 9. Vol. 27. No. 5. pp. 475-482.

A similar fever has already been described in the Congo under the name of "fièvre rouge Congolese." This disease closely resembles measles but Koplik's spots were not present; it differs from dengue in that muscle and bone pains are not marked. [French writers are of opinion that "fièvre rouge" is dengue.] *D. H.*

SHORTT (H. E.), POOLE (L. T.) & STEPHENS (E. D.). **Sandfly Fever on the Indian Frontier. A Preliminary Note on Some Laboratory Investigations.**—*Indian Jl. Med. Res.* 1934. Apr. Vol. 21. No. 4. pp. 775-788. With 5 charts. [10 refs.]

Blood was taken from cases of sandfly fever in Peshawar on the first and second day of the disease and despatched at once to Kasauli where sandfly fever does not occur. Sixty hours later the blood was inoculated into volunteers with the following results:—

	Blood samples	Positive	Typical fever	Modified
1st day ...	10	7	6	1
2nd day ...	4	2	1	1
	14	9	7	2

Six samples of blood were filtered through L3 and L5 Chamberland filters and were found to be infective in three instances.

Sandflies fed on cases of sandfly fever and sent to Kasauli and there fed on volunteers produced a typical attack of fever in one case at least.

Monkeys which had been inoculated with the blood of patients showed a definite rise of temperature and the blood of a monkey taken during the fever produced fever in man. *D. H.*

POOLE (L. T.) & SACHS (Albert). **Preliminary Results of an Investigation into the Aetiology of Sandfly Fever.**—*Jl. Roy. Army Med. Corps.* 1934. Aug. Vol. 63. No. 2. pp. 73-79. [11 refs.]

The strength of the troops in the Peshawar district is about 19,000. In one year as many as 2,000 cases of sandfly fever occurred; this high figure is accounted for by the arrival in the district of troops recently landed from England or from other parts of India where sandfly fever is not prevalent; among "salted" troops the incidence is low.

The object of the present investigation was twofold: (1) to show that the short fever met with in the district is true sandfly fever; (2) to show that the disease is not due to a leptospira or other blood parasite.

Clinically the cases conform to the classical description of sandfly fever; 3 days' fever, slow pulse, flushed face, injected eye, frontal headache, etc.

In a previous investigation in 1932 by one of the authors a spirochaete was discovered in culture from the blood of 3 cases; this resembled *T. pallidum* but with more open coils; it was successfully subcultured.

In 1933 in 470 cases blood taken on the first day of the fever was cultivated in Fletcher's leptospira medium; 0.5 cc. of blood was injected into small capsules containing 4 cc. of the culture medium, the capsules were at once sealed and incubated at 25°C. for 15 days and were then examined and if nothing was found incubated for a further 15 days. In not a single case was a leptospira found; 70 per cent. of the cultures were sterile, the others were contaminated by air-borne organisms; only one capsule contained a pathogenic organism, staphylococcus from a septicaemic case. Direct examination of the blood by dark ground illumination and stained film failed to reveal any organism.

Animal experiments.—Whole blood of cases, cultures after incubation and emulsions of sandflies fed and unfed were injected into rats, rabbits and guineapigs; none developed fever and none showed any sign of disease. Sandflies both fed and unfed were examined by dark ground illumination and by stained smear but no leptospira was seen.

Conclusions.—1. The short fevers of the Peshawar district are sandfly fever. 2. The causal agent is not a leptospira or other visible organism. *D. H.*

RABIES.

A REVIEW OF RECENT ARTICLES. XXII.*

i. *Virus*.

It will be remembered that LEVADITI and SCHOEN (this *Bulletin*, Vol. 31, p. 145) described oxyphil corpuscles which they had observed in the corneal epithelium. As these cells are not neurones though intimately connected with the terminations of the ophthalmic branch of the trigeminal nerve, these authors¹ have examined other ectodermal structures such as the conjunctiva, the nasal mucous membrane, the tongue, and the intestinal mucous membrane. In none of these were oxyphil corpuscles found, though all constitute a favourable place of entry from which the virus of rabies may be dispersed. "From this point of view the corneal epithelium is that which approximates most closely to certain neurones, which in virtue of their neuro-ectodermal origin, facilitate the intracellular evolution of the virus, and thus allows of the development of the visible phase of its cycle of evolution (of the Negri body)."

NICOLAU and KOPCOWSKA² have continued their studies on the effects of rabies virus introduced into the sciatic nerve (this *Bulletin*, Vol. 31, p. 641). They have now directed their attention to the morphogenesis of Negri bodies following this procedure. Negri bodies appear in the neurones of the spinal ganglia of the appropriate segment on the seventh day after infection. The phenomena which precede their appearance have been studied on animals killed at earlier periods. The successive phases of "negriogenesis" are found to be:—(1) agglutination of Nissl granules; (2) flocculation into more or less chromophilic masses; (3) the masses become rounded and more regular and appear to be slightly basophil; (4) these become oxyphilic "under the influence of the germs," and changed in various ways, until they assume the form of Negri bodies. The later changes may be (a) the appearance of a small reddish centre which extends throughout the mass, (b) the masses become more oxyphilic, or (c) a number of oxyphilic points appear, which finally form the "Innenkörper" of the Negri body. "The Negri bodies are formed as a result of the defence of the cell. When inclusions appear in the cell, the cell maintains its morphological and staining integrity. When the cell does not react by the formation of inclusions, the germ multiplies, and degeneration and necrobiosis follow."

From an examination by serial section of the whole brains of 60 mice infected with rabies, and killed at various periods during the course of the disease MURATOWA³ finds that the first appearance of Negri bodies is not in the horn of Ammon, but in the mesencephalon in the neighbourhood of the central canal. Even when the disease is fully

* For the twenty-first of this series see Vol. 31, p. 637.

¹ LEVADITI (C.), SCHOEN (R.) & LEVADITI (J.). Evolution du virus rabique des rues dans les éléments épithéliaux dérivés de l'ectoderme et de l'endoderme.—*C. R. Soc. Biol.* 1934. Vol. 117. No. 34. pp. 767-770.

² NICOLAU (S.) & KOPCOWSKA (L.). Étude sur la morphogénèse des corps de Negri.—*Ann. Inst. Pasteur.* 1934. Oct. Vol. 53. No. 4. pp. 418-437. With 22 coloured figs. on 1 double plate. [Refs. in footnotes.]

³ MURATOWA (A. P.). Ueber die Morphologie des Lyssavirus.—*Zent. f. Bakt. I. Abt. Orig.* 1934. July 2. Vol. 132. No. 1/2. pp. 65-77. With 22 figs.

developed Negri bodies may be absent in the horn of Ammon and in the cerebellum, though present in other parts of the brain. [In this connexion the reviewer would recall the findings of THOMAS and JACKSON and of NICOLAU and KOPCIOWSKA (this *Bulletin*, Vol. 28, p. 744; Vol. 29, p. 600, and Vol. 30, p. 575)]. The author believes that he has observed indications of a definite cycle of development of the parasite of rabies. He believes that the saliva introduced at the time of biting contains very small structures either free or in the form of the *Innenkörper* of the Negri body. In the muscle the parasite becomes enclosed in a thick membrane and under favourable circumstances reaches a nerve ending. It passes along the nerve to the brain, and becomes freed from its envelope. The freed forms then divide and (mainly in the medulla) form morulae. These spread through the brain, probably along the blood vessels, and penetrate the nerve culls. At this stage they are basophilic, but later they become oxyphilic and take the form of Negri bodies. At a later stage the "*Innenkörper*" are freed and spread to other parts of the brain forming new Negri bodies. The article is illustrated.

The effect of low temperatures on the virus of rabies has been studied by REMLINGER and BAILLY.⁴ They find that when kept in the refrigerator in a frozen state, fixed virus maintained its virulence up to 768 days, and street virus up to 775 days. Also a brain kept in glycerine at + 6°C. remains virulent after 901 days.

It may be remembered that NICOLAU and KOPCIOWSKA (this *Bulletin*, Vol. 28, p. 247) showed that the virulent moiety of rabies brain emulsion is negatively charged and migrates during cataphoresis towards the positive pole, and that GLUSMAN, GORFUNKEL and SSOLOWIEWA (*loc. cit.*, Vol. 29, p. 195) confirmed this observation. The pH range within which this phenomenon was observed was in the case of the former observers between 6.0 and 9.3, and in the case of the latter between 5.8 and 7.4. Further observations are now put forward by SANKARAN, IYENGAR, and BEER,⁵ and MCCARRISON, SANKARAN and BEER⁶. These were carried out at a pH of 7.38. Thirty of 33 animals inoculated with material collected from the positive cell developed rabies, whereas none of 33 inoculated with material from the negative cell died. GLUSMAN and his co-workers found no evidence of a separation of the virus from the material to which it is attached. MCCARRISON and his colleagues have found evidence of a considerable degree of separation. The matter is complicated by the fact that at a pH in the neighbourhood of 7.3 most proteins carry negative charges.

The action of various pancreatic ferments on rabies virus has been examined by HIRANO.⁷ He finds that the virus is destroyed completely by a 4,000 fold dilution of lipase, and incompletely by an 8,000 fold dilution. The virus on the whole resists the action of trypsin and

⁴ REMLINGER (P.) & BAILLY (J.). Action de la congélation sur le virus rabique.—*C. R. Soc. Biol.* 1934. Vol. 116. No. 20. pp. 407-409.

⁵ SANKARAN (G.), IYENGAR (K. R. K.) & BEER (W. A.). A Preliminary Note on the Electrical Charge carried by the Rabies Virus.—*Indian Jl. Med. Res* 1934. Apr. Vol. 21. No. 4. pp. 909-916. With 2 figs.

⁶ MCCARRISON (Robert), SANKARAN (G.) & BEER (W. A.). Electrophoresis Experiments with the Virus of Rabies.—*Indian Jl. Med. Res.* 1934. Apr. Vol. 21. No. 4. pp. 917-934.

⁷ HIRANO (Norimasa). On the Resistance of Rabies Virus to the Action of Some Ferments.—*Kitasato Arch. Experim. Med.* 1934. July. Vol. 11. No. 3. pp. 246-252.

diastase, though in low dilution it may be influenced by these ferments. It was not possible to demonstrate the action of pepsin, as it was found that the virus was completely destroyed by the action of 0.01 per cent. hydrochloric acid alone, at 37°C. for two hours. The author concludes that "the rabies virus is composed mainly of a substance which is easily decomposed by pancreatic lipase."

JANSEN⁸ has succeeded in transmitting the virus of the pseudorabies of AUJESZKY through 17 passages in the mouse by intracerebral inoculation. The inoculation period was at first 4½ days, and finally was reduced to 3 days. In every case the animal died of the disease. Itching was not an invariable symptom but it was observed in a considerable proportion of the cases. Subcutaneous inoculation into other mice in no case transmitted the infection, but when large doses were given they conferred some degree of immunization. It is the intention of the author to continue this series up to 100 passages.

HURST⁹ has continued his study of pseudorabies (this *Bulletin*, Vol. 31, p. 146). From a series of experiments he shows that the Iowa strain of virus reaches the nervous system by way of the peripheral nerves, although it is circulating also in the blood. For example he found that the salivary glands are often infective after intracerebral inoculation or after subcutaneous inoculation into the base of the ear, and rarely if infection is practised subcutaneously in the flank or foot. The adrenals are frequently infective after subcutaneous inoculation into the flank, but not after injection into the leg or ear. Centrifugal spread from the infected nervous tissues by the neural route also occurs. The Aujeszky strain invades the blood stream more readily than does the Iowa strain, but possibly after repeated passage the latter is approximating in this respect more closely to the classical Aujeszky strain. After intravenous inoculation, effective with even small doses, virus is rapidly removed from the blood, and multiple infective foci are established in various organs; thence ascent of the virus by the peripheral nerves leads to infection of the central nervous system. No evidence has been found that the virus can penetrate the haemato-encephalic barrier directly. After subcutaneous inoculation into an area deprived of its nerve supply, the ability of the virus to invade the blood permits it to establish infective foci in the various viscera, and after a predictable delay, the course of infection resembles that following intravenous injection. The virus is pantropic, *i.e.*, it readily attacks cells derived from any embryonic layer.

Following upon a summary of their experiments on the virus of the pseudorabies of AUJESZKY (this *Bulletin*, Vol. 31, p. 639) REMLINGER and BAILLY¹⁰ discuss the nature of this virus in the light of these experiments. There are three possibilities, (1) it may be a protozoon, having a cycle of evolution one stage of which is filtrable; (2) it may be a very minute bacterium; or (3) it may be an enzyme. The facts are

⁸ JANSEN (Jac.). De gevoeligheid van de muis voor het virus van de ziekte van Aujeszky.—*Tijdschr. v. Diergeneesk.* 1934. July 15. Vol. 61. No. 14. pp. 761-763. English summary (9 lines).

⁹ HURST (E. Weston). Studies on Pseudorabies (Infectious Bulbar Paralysis, Mad Itch). II. Routes of Infection in the Rabbit, with Remarks on the Relation of the Virus to Other Viruses affecting the Nervous System.—*Jl. Experim. Med.* 1934. June 1. Vol. 59. No. 6. pp. 729-749. [28 refs.]

¹⁰ REMLINGER (P.) & BAILLY (J.). Contribution à l'étude de la nature du virus de la maladie d'Aujeszky.—*C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 409-411.

that the virus is filtrable, is diffusible, is not brought down by centrifugation, and can reproduce the disease in series. The diffusibility excludes the virus from the protozoa and the bacteria, and brings it into approximation with chemical substances. In agreement with this view is the insensitiveness of the virus to centrifugation. The virus, however, can only traverse porcelain filters of a certain porosity, and has in addition the property of reproducing the disease in series, a property which is possessed by bacteria. The authors ask themselves whether it is possible that the virus occupies an intermediate position between the visible microbes and the diastases. REMLINGER has made a similar suggestion with regard to the virus of rabies (*Bull. Acad. Méd.* 1918, Vol. 79, p. 137).

A strain of the virus of Aujeszky has been isolated in Rumania by JONNESCO.^{11, 12} Its properties are described. It was transmitted to the cock. In one case an inoculated cock developed symptoms 72 hours after infection. These persisted for 5 days, after which the animal recovered. The blood of this animal inoculated intracerebrally into rabbits reproduced the disease in a fatal form. Various pathological observations are recounted. In dogs a marked leucocytosis was observed, the white cells numbering 27,000 per cubic millimetre; a differential count showed 62 per cent. of polymorphs, 4 per cent. of neutrophil metamyelocytes, 8 per cent. of lymphocytes, 12 per cent. of monocytes, and 5 per cent. of plasma cells. The polymorphs contained few granules, and showed degenerative changes. The histological appearances in the tissues are also described.

ii. Symptomatology and Diagnosis.

WINTER¹³ reports upon an outbreak of rabies amongst animals in Barrackpore (Bengal) upon which one fatal case of hydrophobia in a woman supervened. In her case the period of incubation was 41 days; as she had not been bitten and she stated that she had not been licked, no treatment was given. Further evidence, however, showed that she had in all probability been licked.

JONNESCO¹⁴ compares results obtained by subdural inoculation of 0.2 cc. of rabid brain emulsion into rabbits, with those obtained by intracaudal inoculation of 0.1 cc. of the same emulsion into mice. In all cases the emulsion contained street virus. The results were as follows. By subdural inoculation of 30 rabbits, 3 became paralysed in less than 7 days, 12 between the 8th and the 15th days, 11 between the 16th and the 28th days, and 4 between the 28th and the 48th days. Of 56 intracaudally inoculated mice 3 became paralysed in less than 7 days, 38 between the 8th and 15th days and 10 between the 16th and 28th days. He therefore recommends the latter method as being almost as sure, more economical, and often more rapid than the former. Two mice should be inoculated on each occasion.

¹¹ JONNESCO (Démètre). Recherches sur la maladie d'Aujeszky.—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. pp. 1184–1186.

¹² JONNESCO (Démètre). Contribution à l'étude de la maladie d'Aujeszky.—*Ann. Inst. Pasteur.* 1934. Nov. Vol. 53. No. 5. pp. 554–563.

¹³ WINTER (H. G.). Hydrophobia.—*Jl. Roy. Army Med. Corps.* 1934. Aug. Vol. 63. No. 2. pp. 122–125.

¹⁴ JONNESCO (Démètre). Diagnostic de la rage au moyen de l'inoculation intracaudale chez la souris.—*C. R. Soc. Biol.* 1934. Vol. 116. No. 21. pp. 545–548. With 1 chart.

iii. Pathology.

The histological appearances in the brains of 16 cases of human rabies are described by VERHAART.¹⁵ In all cases there was severe inflammation in the medulla oblongata and the pons, in particular in the tegmentum, the cranial nerve nuclei, and the reticular nuclei. In one atypical case with a prolonged course, the olive and the pes pontes were more affected than the tegmentum. Of the 16, 2 showed definite, and 7 slight, inflammation in the mesencephalon, in particular in the red nucleus, and the corpora quadrigemina, whilst in one case the substantia nigra was alone affected. No inflammation was observed in the diencephalon unless the mesencephalon was also affected, nor in the mesencephalon unless the pons and medulla were also affected. The inflammation took the form of perivascular and diffuse infiltration by lymphocytes, polymorphonuclear leucocytes, and enlarged microglia.

The effects of various processes which affect the haemato-encephalic barrier have been studied by FUNAYAMA.^{16, 17} Injection into the sub-arachnoid space of horse serum, dog serum, a 5 per cent. solution of sodium aleuronate, or purpuring, along with intracerebral injection of various fixed virus strains, did not induce rabies in the case of strains of fixed virus of incubation 5 and 6 days, but induced symptoms in an 8-day strain. It was also noted that "the alteration in the haemato-encephalic barrier had no effect on fixed virus which had been introduced into the circulation."

REMLINGER and BAILLY¹⁸ extend their observations on the presence of rabies virus in the lung (this *Bulletin*, Vol. 31, p. 640). They have now succeeded in demonstrating its presence 9 times out of 24, *i.e.*, 37.5 per cent. The lung must thus possess a sufficient number of infected neurones to produce these infections. They may be situated in the nerve endings of the muscular and mucous coats of the bronchioles, in the nerve endings in the vessel walls, or in those in the alveolar epithelium described by RETZIUS.

MATSUDA¹⁹ has carried out a series of experiments on the irritability of the intestinal sympathetic and parasympathetic nerve endings during the course of infection with rabies virus. He ascribes the results which he obtained to the presence of inflammation in the intestinal canal, and to invasion by the virus of the whole nervous system from the nerve centres down to the nerve endings. As regards the parasympathetic, half the cases were sensitive to acetyl choline and atropine; as regards the sympathetic, half were in the early stages sensitive to

¹⁵ VERHAART (W. J. C.). De encephalitis bij de menschelijke lyssa.—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. May 22. Vol. 74. No. 11. pp. 681-687. German summary.

¹⁶ FUNAYAMA (Jün-Itchi). Contribution à l'étude de la rage expérimentale.—*Oriental Jl. Dis. Infants*. 1934. May. Vol. 15. No. 3. [In Japanese. [24 refs.] French summary pp. 43-46.]

¹⁷ FUNAYAMA (Jün-Itchi). Contribution à l'étude de la rage expérimentale.—*C. R. Soc. Biol.* 1934. Vol. 116. No. 26. pp. 1170-1172.

¹⁸ REMLINGER (P.) & BAILLY (J.). Sur la présence du virus rabique dans le poupon.—*Ann. Inst. Pasteur*. 1934. July. Vol. 53. No. 1. pp. 43-50.

¹⁹ MATSUDA (Shoitsu). The Contribution to the Knowledge of the Experimental Rabies. (Report I.) The Investigation of the Intestinal Canal of Rabid Rabbits. 1. The Change of the Irritability of Autonomous Nervous System and Involuntary Muscle in Intestinal Canal of Rabid (Hydrophobic) Rabbits.—*Oriental Jl. Dis. Infants*. 1934. July. Vol. 16. No. 1. [In Japanese. English summary pp. 1-4.]

adrenaline, this sensitiveness disappearing as paresis set in. Further observations on the sympathetic nerve endings of the vessels indicated an increase in sensitiveness, which in certain cases weakened as paresis set in. [This précis is made from an English summary which is difficult to interpret, and its accuracy cannot be vouched for.]

iv. *Methods of Treatment and Statistics.*

During the year 1933, 132 cases of persons bitten by dogs have been reported in Germany,²⁰ as compared with 64 in the previous year. Of the 132, 2 died of rabies, and in neither case had treatment been given. Actually 153 persons were treated during the year, 47 in Berlin, 97 in Breslau, 1 in Munich, and 8 in Dresden. Of these none contracted rabies, and no paralytic nor other sequelae were observed. Attention is drawn to the increase in the prevalence of rabies in Germany, and especially in the Eastern districts bordering on Poland and Czechoslovakia.

VIALA²¹ reports that during the year 1933, 443 persons were treated at the Pasteur Institute at Paris. There were no failures of treatment, nor were any post-vaccinal sequelae observed.

v. *Rabies in Animals.*

REICHEL and SCHNEIDER²² recommend intra-lingual inoculation of the test dose in estimating degree of immunization. They consider a protection test to be satisfactory when at least 60 per cent. of the vaccinated animals survive, while 60 per cent. or more of the controls die of the intra-lingual infecting dose. From a series of experiments on rabbits they found that when given in single doses, formalin-killed and autoclave-killed vaccines failed to pass the test, whilst live vaccine, chloroform-killed and phenol-killed vaccines all passed the test.

In a second communication²³ the test is further applied. Treatment for 14 days with both carbolized and chloroform treated vaccines gave adequate protection. They then compared the immunizing properties of carbolized vaccines kept at room temperature for various periods. The results of this experiment are as follows:—

Date of preparation of vaccine.					Number treated	Died of rabies
1929	5	5
1930	5	5
1931	4	1
1932 (1st 6 months)	3	0
1932 (2nd ")	4	0
1933	5	2
Normal rabbit brain	4	3
Controls	35	29

(Doses of 2 cc. of a 5 per cent. emulsion were given daily for 7 days in each case.)

²⁰ REICHS-GESUNDHEITSBLATT. 1934. Oct. 31. Vol. 9. No. 44. pp. 932-933.—Die Tätigkeit der deutschen Wutschutzstationen im Jahre 1933.

²¹ VIALA (Jules). Les vaccinations antirabiques à l'Institut Pasteur en 1933.—*Ann. Inst. Pasteur*. 1934. June. Vol. 52. No. 6. pp. 709-713.

²² REICHEL (John) & SCHNEIDER (J. E.). Rabies Vaccine Protection Test.—*Jl. Amer. Vet. Med. Assoc.* 1934. May. Vol. 84. No. 5. pp. 752-756.

²³ REICHEL (John) & SCHNEIDER (J. E.). Rabies Vaccine Protection Tests.—*Amer. Jl. Pub. Health*. 1934. June. Vol. 24. No. 6. Pt. 1. pp. 625-628.

The authors conclude that "Rabies vaccine (phenol killed) kept at room temperature for 2 years satisfactorily passed the protection test, supporting the contention that rabies vaccine can be dated for 2 years from the date of issue."

The effects of single dose administration of various vaccines as a prophylactic against rabies have been examined by BARNES, METCALFE, MARTINDALE and LENTZ.²⁴ The conclusions arrived at are stated to be tentative. They found that administration of single doses of 4 carbolyzed vaccines to 4 groups of 10 dogs gave no protection—"33 of the total of 40 contracted rabies (*i.e.*, 82.5 per cent.) whereas 13 of 16 untreated succumbed (81.3 per cent.)." A second series of experiments in which chloroform treated vaccine was used gave "somewhat more encouraging results, but not sufficient to warrant confidence in it to the exclusion of police and sanitary measures." In this case, of 20 vaccinated dogs 7 (35 per cent.) died of rabies, whereas of 20 controls 11 (55 per cent.) succumbed.

vi. *Post-vaccinial Paralyses.*

A fatal case of transverse myelitis following antirabic treatment at the Instituto de Semiología (Argentina) is described by UDAONDO, SANGUINETTI, and ZUNINO.²⁵ The patient was a veterinary surgeon. He had been in contact with a dog suffering from furious rabies, but had not been bitten or scratched by it. He had disinfected his hands immediately after he had handled the animal. He commenced treatment 8 days after, and 14 days thereafter symptoms set in. These were mainly of the nature of an ascending anaesthesia, with paralysis of the lower limbs. After an illness of seven days the patient died, and the histological appearances (which are illustrated) were those of a subacute necrotic transverse myelitis in the cervical region. A discussion of the aetiology of paralytic accidents follows.

MARINESCO and DRAGANESCO²⁶ discuss a case of paralytic accident which exhibited the symptoms of the Landry type and terminated fatally. The patient had been treated by heated emulsions according to the method of Babes. Symptoms appeared on the 15th day and death followed 5 days later. The tissues were examined. Rabbits inoculated subdurally with the nerve tissue developed paralysis on the third day and died after the 5th or 6th day. The authors draw attention to the view of REMLINGER that cases in which the presence of rabies virus is proved by animal experiment should be excluded from the category of paralytic accident, and should be ascribed to errors of manipulation in the laboratory. The authors do not, with regard to this particular case, subscribe to this generally accepted view. They state that this virus vaccine, though admittedly virulent, has been employed without ill effects on a large series of cases. They suggest that in this case a reinforced strain of street virus may have been operating.

²⁴ BARNES (M. F.), METCALFE (A. N.), MARTINDALE (W. E.) & LENTZ (W. J.). Canine Rabies Experimental Vaccination. Second and Third Reports.—*Jl. Amer. Vet. Med. Assoc.* 1934. May: Vol. 84. No. 5. pp. 740-751.

²⁵ UDAONDO (C. Bonorino), SANGUINETTI (Lucio V.) & ZUNINO (Livio V.). Mieltis mortal por vacunación antirrábica.—*Prensa Méd. Argentina.* 1934. Aug. 22. Vol. 21. No. 34. pp. 1565-1570. With 3 figs. [22 refs.]

²⁶ MARINESCO (G.) & DRAGANESCO (St.). Étude anatomoclinique et expérimentale d'un cas d'encéphalomyélite rabique survenue au cours d'un traitement pasteurien.—*Bull. Acad. Méd.* 1934. July 31. 98th Year. 3rd Ser. Vol. 112. No. 29. pp. 181-189.

vii. *Miscellaneous.*

PROCA, BOBES and JONNESCO²⁷ have continued their studies in which they employ intraplantar inoculation as the mode of transmission (this *Bulletin*, Vol. 31, p. 642). This method is peculiarly suitable for the study of the effects of local treatment. They find that, when antirabic serum is injected in the same locality, it has a definite preventive action; twelve out of sixteen treated animals survived. When formate and salicylate of sodium were added to the serum the action of the serum was reinforced, but on the contrary the action was diminished when the serum was kept for some time in dilution in the presence of an anti-septic, such as phenol, formate or salicylate of soda.

GONZÁLEZ²⁸ continues the memoir on rabies, the earlier part of which has already been reviewed, by a section on the clinical aspects of fatal human cases. Twenty-eight case histories dating from 1919 to 1931 are given in detail.

A. G. McKendrick.

²⁷ PROCA (G.), BOBES (S.) & JONNESCO (D.). Sur quelques essais de séro-thérapie locale de la rage.—*C. R. Soc. Biol.* 1934. Vol. 117. No. 28. pp. 133-135.

²⁸ GONZÁLEZ (Hernán D.). La rabia humana.—*Semana Méd.* 1934. May 3. Vol. 41. No. 18 (2103). pp. 1373-1395. With 26 charts. [59 refs.]

TROPICAL DERMATOLOGY.

A REVIEW OF RECENT ARTICLES. I.

Blastomycosis.—CASTELLANI and JACONO¹ have analysed the characteristic features of fungi isolated from cases seen in North America and Europe. In dealing with the vexed question of diagnosis they make the following definition :—" The term 'blastomycosis' is used to indicate any disease due to fungi, which appear in the lesions as roundish or oval cells, at times budding, *with complete absence of mycelium*." Under this ruling there are two main types ; (1) Blastomycoides with well-defined membranes, double contours and well-marked fat-droplets ; (2) Cryptococcoid type of smaller cells with the double contours much less marked and the spherules finer. In the series under discussion there were SIX cases of pulmonary and 23 of dermal infection. Full histological and cultural details are given of the 25 fungi isolated, the five principal organisms being *Geotrichum immite*, *G. dermatitidis*, *Monosporium tulanense*, *Glenospora lanuginosa* and *Acrotheca pedrosoi*. The paper also includes an account of the experimental results obtained in skin tests with a blastomycetin, prepared in the same way as old tuberculin. In experimentally infected rats scratch and intradermic tests always gave positive flares. Seven healthy controls gave negative results whilst four affected patients yielded two positive and one doubtful reactions. REDAELLI and CIFERRI² studied the cultural, morphological, biochemical and pathogenic properties of four strains obtained from cases of Gilchrist's disease seen in North and South America. These fungi had been labelled *Endomyces dermatitidis*, *E. capsulatus* Rewbridge, *E. capsulatus* var. *isabellinus* and *Blastomyces gilchristi*. They seemed to be identical. The authors examine the whole genus *Blastomyces* and as a result separate a genus to which they give the name *Gilchristia dermatitidis* and which has eleven different synonyms. This group differs from the *Endomyces* in the possession of 8-spored asci, absence of fermentative power, cultural reversible dimorphism, etc. ROTTER and CHAVARRIA³ describe three cases seen in Costa Rica. The first occurred in a 70-year old agricultural labourer. The appearance presented by the right hand and forearm were clinically typical. There was no glandular involvement and *Hormodendron langeroni* was cultivated. In a male negro lesions first appeared round the mouth and thence gradually spread to the neck and back. The case corresponded in every way to those described as Brazilian Paracoccidioidosis. The third case is interesting in that the lesions occurred on the forehead shortly after a wasp sting in that area.

¹ CASTELLANI (Aldo) & JACONO (Igino). Observations on Fungi isolated from Cases of Blastomycosis Cutis and Blastomycosis Pulmonalis in North America and Europe. Remarks on Blastomycetin.—*Jl Trop. Med. & Hyg.* 1933. Oct. 16. Vol. 36. No. 20. pp. 297-321. With 56 figs. & 1 coloured plate. [76 refs.]

² REDAELLI (P.) & CIFERRI (R.). *Gilchristia dermatitidis* (Gilchr. et Stokes) Cif. et Red., the Causative Agent of the American Gilchrist Disease (Dermatitis Verrucosa).—*Jl Trop. Med. & Hyg.* 1934. Sept. 15. Vol. 37. No. 18. pp. 280-282. [21 refs.]

³ ROTTER (Werner) & CHAVARRIA (A. Peña). Weitere Untersuchungen ueber Blastomykosen in Costa Rica.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Oct. Vol. 38. No. 10. pp. 406-417. With 11 text figs.

New patches of infection have since involved the right ear and neck. The causative organism in this case is to be the subject of a later communication.

Lymphostatic verrucosis.—LOEWENTHAL⁴ has also endeavoured to clarify the confusion which exists in our knowledge of the fungus diseases. He deals in particular with "Mossy foot," Dermatitis verrucosa and verrucosis associated with chronic oedema, a name given to cases seen in Uganda. He studies this last type in particular and describes 11 such examples. These have a prodromal stage of "velvet" skin, succeeded by oedema and sharply defined verrucosity. There is no tenderness, but ulceration and fibromata occur later. In eight of the cases no cause could be found for the oedema apart from the local lesion. Microscopically there are no giant-cells and no obvious organisms. For this Uganda type he suggests the name "Lymphostatic verrucosis." In "Mossy foot" the presence of an organism is also probable but unproven, but the clinical features serve to distinguish the two diseases, whilst dermatitis verrucosa is of course a synonym for blastomycosis.

Mycetoma.—MONTPELLIER and CATANEI⁵ obtained material from the amputated foot of a native in Algiers. There was a regular swelling of the ankle which had existed for several months, together with some cicatricial nodules and others of a dirty grey colour containing small abscess cavities. The organism proved to be *Acremonium potroni*. With GOINARD⁶, CATANEI describes a second case in a native male aged 30. Here the foot showed diffuse swelling, particularly of the sole on which there were 30 or so small brownish papules, a few fistulae and some scarring. *Allescheria boydii*, Shear 1921, was isolated. In his third publication CATANEI⁷ adds a third example, this time in a male native 40 years of age. When seen, five years after onset, there was hypertrophy of the dorsum of the foot with numerous nodules of varying induration and some fistulae. *Nocardia madurae* was proved to be responsible, as is usually the case in Algeria. Another case is reported from Brazil by GONZAGA & LEÃO.⁸ A man, 24 years of age, who had lived practically all his life in S. Paulo developed small subcutaneous nodules near the tibial tuberosities of both legs. These were painful and attached to the skin, but were movable over the deeper tissues. The lesions on the left leg broke down to form ulcers discharging a yellowish, viscid pus. The patient became pale and weak, whilst the spleen could be felt three fingers' breadths below the costal margin. The presence of fungus was proved. The article also

⁴ LOEWENTHAL (L. J. A.). On the Probable Inclusion of Several Diseases in the Title "Mossy" Foot.—*Ann. Trop. Med. & Parasit.* 1934. Mar. 29. Vol. 28. No. 1. pp. 47-62. With 5 figs. (2 coloured) on 3 plates. [37 refs.]

⁵ MONTPELLIER (J.) & CATANEI (A.). Résultats de l'étude d'un nouveau mycétome du pied observé à Alger.—*Bull. Soc. Path. Exot.* 1934. Mar. 14. Vol. 27. No. 3. pp. 209-214. With 1 fig.

⁶ CATANEI (A.) & GOINARD (P.). Un nouveau cas algérien de mycétome du pied.—*Bull. Soc. Path. Exot.* 1934. Feb. 14. Vol. 27. No. 2. pp. 176-178. With 2 figs.

⁷ CATANEI (A.). Étude parasitologique de trois mycétomes du pied observés en Algérie, en 1933.—*Arch. Inst. Pasteur d'Algérie.* 1934. June. Vol. 12. No. 2. pp. 169-180. With 7 figs. & 1 plate.

⁸ GONZAGA (A. Gavião) & LEÃO (A. E. Arêa). Acremoniose (mycose por acremonium).—*Rev. Med.-Cirurg. do Brasil.* 1934. Jan. Vol. 42. No. 1. pp. 24-32. With 12 figs. (11 on 4 plates).

contains histological and cultural details, etc., of the two species *Acremonium mulhuoni* and *A. potroni*.

Actinomycosis.—A very well-illustrated article by CH'IN⁹ describes three cases seen in Peiping, China. A Greek farmer, aged 55 years, gave a six months' history of fever and cough. Empyema necessitated thoracostomy which left the patient with thickened pleura and some fluid in the left chest. Scarring was present together with a few sinuses discharging a thin, yellowish, foul pus. Death ensued despite treatment and it was only post-mortem that the fungus was found in abscesses of the pleura and lung. The second case occurred in a Chinese girl student, aged 22, who had had some swelling of the right side of the face for five weeks. There were no sinuses, but X-rays revealed osteomyelitis of the mandible. The lesion was incised and drained, typical granules being found in the pus. Lugol's solution was given by mouth and local treatment with radium was instituted. Rapid healing followed and there was no relapse six months after the cessation of treatment. Finally there is described the case of a Russian housewife, aged 45, who developed a local swelling two months after appendicectomy. A second laparotomy revealed a large, inoperable mass attached to a sinus which was present at the lower end of the original scar. Pus obtained from this sinus and from the mass post-mortem contained typical ray fungi which proved to be *Nocardia bovis* on culture.

Piedra.—BRUMPT and LANGERON¹⁰ have examined material sent from Venezuela. The specimen proved too old for culture but they are of the opinion that, on histological grounds, the fungus constitutes a new species. They propose to name it *Piedra venezuelensis*. The authors also discuss the microscopical appearances presented by *P. hortai* and *P. sarmentoi*, and demonstrate that in these fungi the asci contain eight ascospores, whereas in the new species only four are present. A general historical review points out that this malady differs from Trichomycosis in that the small sand-like nodules are found almost exclusively on the hairs of the scalp. In South America the nodules are dark in colour, whereas they are light in cases occurring in the Old World, where *Trichosporum* is responsible.

Tinea tonsurans.—A preliminary statistical note on the incidence of ringworm of the scalp in Spanish Morocco is presented by BAEZA.¹¹ Children, adolescents and native troops were examined. Of 2,708 persons thus inspected 304 were proved to be infected with favus, 156 with *Trichophyton violaceum*, three with *T. sulphureum* and one with both these latter fungi. Of the 464 infections, 393 occurred in small boys, 52 in youths, 12 in girls, and 7 in soldiers. The author nowhere notes the site of the infection but it is presumed that he is dealing with the scalp. The following three points are worthy of note: the absence of microsporon infections, the high percentage of favus and the small

⁹ CH'IN (T. L.). A Mycological Study of a Case of Actinomycosis with a Report of Three Cases observed in North China —*Chinese Med. Jl.* 1934. June. Vol. 48. No. 6. pp 551-562. With 10 figs. on 4 plates. [25 refs.]

¹⁰ BRUMPT (E.) & LANGERON (M.). Considérations sur la piedra de l'Amérique du Sud, à l'occasion d'un cas provenant du Venezuela. Description d'une espèce nouvelle *Piedraia venezuelensis* n. sp.—*Ann. Parasit. Humaine et Comparée.* 1934. Mar. 1. Vol. 12. No. 2. pp. 134-161. With 32 figs. & 1 plate. [33 refs.]

¹¹ BAEZA (M.). Note statistique préliminaire sur les teignes du Maroc espagnol.—*Ann. Parasit. Humaine et Comparée.* 1934. Sept. 1. Vol. 12. No. 5. pp. 405-407.

variety of fungi. The paper by ALDICK¹³ deals with an outbreak of *Microsporon audouini* cases in Schleswig-Holstein. There were seen 301 cases of scalp disease, 10 per cent. of the patients also showing lesions of the glabrous skin. The importance of this paper lies in the apparent simplicity and efficiency of the treatment. In pure chloroform there is dissolved 2 per cent. of absolute acohol and 1 per cent. of cinnamyllic acid. The scalp is painted three times a day with this lotion, care being taken to prevent contact with the eyes. Cure occurred in four to five weeks in the vast majority of cases. Failure is reported in 4.3 per cent. of boys and in 14.2 per cent. of girls, whose longer hair was apparently never cut in this series.

Tinea circinata.—KAMBAYASHI¹³ reports the laboratory findings in material obtained from a 12-year old Chinese boy living near Shanghai. The lesions are described as typical of *T. circinata* and were situated on the right ala nasi and temple. Very detailed observations are given of the histological and cultural features of the fungus, which also proved pathological to guineapigs on subcutaneous and intraperitoneal inoculation. The organism is very like that described in 1925 by the authors whose names are attached to its title, *Malbranchea Bolognesi-Chiurcoi* Vuillemin.

Tinea imbricata.—After tracing the history of this disease from Malaya to the adjacent countries, ACTON & GHOSH¹⁴ give details of the first definite example to be recognized in India. This occurred in a Bengali youth, aged twenty, who acquired the malady in childhood. He had never left his home district, which is bordered by the Garo hills, but it is possible that he gained his infection by direct contact with visitors from these hills. The case was at first thought to be one of generalized exfoliative dermatitis, but careful examination revealed some concentric rings on the back. Culture was successful but inoculation into guineapigs failed. A volunteer was, however, infected by rubbing an emulsion of the culture into a scarified area of the forearm. It is pointed out that the cultural characteristics vary very greatly both with the medium used and with the oxygen supply. The authors consider that CASTELLANI's creation of the genus *Endodermophyton* is unnecessary. As this particular fungus showed features common to both *E. tropicale* and *E. indicum*, they suggest the name *Achorion indicum*, Castellani 1911. It is possible, however, that all four endophyta are but a single species (i.e., *E. concentricum* and *E. mansonii* in addition to the above). If this is proved, the organism should be called *A. concentricum*, Blanchard 1901.

Epidermophytosis.—NIÑO¹⁵ describes a typical case in a Spaniard, the sole of whose left foot was affected. The majority of the lesions were between and near the toes and also on the heel. It is stated that

¹³ ALDICK (W.). Ueber eine Mikrosporiepidemie in Schleswig-Holstein und ihre Behandlung mit Zimtchloroform.—*Arch. f. Dermat. u. Syph.* 1934. Sept. 14. Vol. 170. No. 4. pp. 473-484. With 6 figs.

¹³ KAMBAYASHI (T.). Ueber ein von einer Spezies der *Malbranchea* hervorgerufenes Hautleiden in China.—*Arch. f. Dermat. u. Syph.* 1934. Apr. 20. Vol. 170. No. 1. pp. 97-106. With 50 figs.

¹⁴ ACTON (H. W.) & GHOSH (L. M.). *Tinea Imbricata* (Tokelau) in Bengal.—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 426-430. With 2 plates (1 coloured).

¹⁵ NIÑO (Flavio L.). *Epidermoficia plantar dishydrosiforme*.—*Bol. Inst. Cln. Quirúrg.* 1934. Vol. 10. Nos. 82 & 83. pp. 21-24. With 12 figs.

the condition cleared up after being painted with Tr. Iodi and Biodermol. Culture proved the fungus to be *Epidermophyton floccosum*, Harz. SOUTER¹⁶ discusses his experiences in Hong-Kong itself. In cases where secondary infection has occurred it is his custom to deal with this first by means of a staphylococcal antiviral. Thereafter cleanliness and clearance of dead skin are essential. These aims being achieved, Mycosil is most useful. Whitfield's lotion and Castellani's paint earn equally high praise. In the succeeding paper of the same journal, HAYES¹⁷ describes the condition as seen in South Africa. The treatment there recommended is a paint of brilliant green in a strength not exceeding 10 per cent.

Moniliasis.—The intradermic reactions caused by levurine and by a similar monilial preparation are discussed by NEGRONI.¹⁸ Agglutination and intradermic tests both proved unreliable, both false negatives and false positives being given. Complement fixation tests were, however, positive in 38 out of 50 cases.

Streptococcal dermatitis.—OTHAZ¹⁹ records his results in 54 patients suffering from "streptococcal infections of the skin" who were treated by means of intravenous injections of ammoniacal copper sulphate. At first the daily dose consists of 0.02 to 0.04 gm.; this is gradually increased to 0.06 or 0.08 gm. Larger doses require an interval of 48 hours between each. It is stated that the method is satisfactory and that no other local or general measures are required.

Lupus erythematosus.—Five cases in the Philippines are described by HASSELMANN²⁰; of these, three were Japanese, one an American and the other a native girl. Only this last example is noted in detail. She had a typical lesion of the left buttock which cleared up on gold injections and local painting with Tr. Iodi. The histology was atypical in that a lymphoid cellular infiltration was more marked than is usual and some Langhan's giant cells were seen although no tubercles were present. There were no apple-jelly nodules, and no relapse occurred during two years' observation.

Colour Changes.—A most instructive article has been written by LOEWENTHAL²¹, who first considers the normal variations in the distribution of pigment in the African's skin, e.g., the usual lighter shades seen over the clavicles, thoracic spine, supraorbital ridges, tip of nose, etc. Pathological pallor can be produced by "masking," an effect resultant on the presence of hyperkeratosis, oedema, stretching and circulatory disturbances of the skin. The actual amount of pigment

¹⁶ SOUTER (J. C.). A Practical Note on Hong Kong Foot, or Dhoobie Itch.—*Jl. Roy. Nav. Med. Serv.* 1934. Oct. Vol. 20. No. 4. pp. 369-372.

¹⁷ HAYES (G. H.). Epidermophyton Infection or Athlete's Foot.—*Jl. Roy. Nav. Med. Serv.* 1934. Oct. Vol. 20. No. 4. pp. 372-373.

¹⁸ NEGRONI (Pablo). Réactions biologiques dans les monilioses cutanéomucqueuses. Leur valeur comparative.—*Rev. Sud-Américaine de Méd. et de Chirurg.* Paris. 1934 Feb Vol 5 No. 2 pp. 65-74.

¹⁹ OTHAZ (Ernesto L.). Tratamiento de las enfermedades estreptococcicas de la piel por el sulfato de cobre amoniacal endovenoso.—*Semana Méd.* 1934. June 7. Vol. 41. No. 23 (2108). pp. 1734-1743. With 10 figs.

²⁰ HASSELMANN (C. M.). Lupus Erythematosus (Discoideus) in the Tropics. First Report of Cases from the Philippine Islands and Investigations on the Occurrence of Langhan's Giant Cells.—*Arch. Dermat. & Syph.* 1934. Apr. Vol. 29. No. 4. pp. 585-596. With 6 figs. [20 refs.]

²¹ LOEWENTHAL (L. J. A.). The Significance of Colour Changes in the African Skin.—*East African Med. Jl.* 1934. July. Vol. 11. No. 4. pp. 124-131. With 2 figs. [22 refs.]

may be reduced after inflammation has subsided, in neurotrophic lesions, etc. Circulatory changes having this effect are caused by the fevers, pityriasis rosea and urticaria. The mycoses nearly all produce relative pallor, as also do vitiligo, leprosy, late yaws, etc. On the other hand darkening results from extraneous colouring, an increase in melanin or keratin and as a sequel to folding of the epidermis. Exposure to sun and pregnancy are included in the physiological causes, whilst moles are of course congenital. Extraneous agents include chemicals and *Tinea nigra*. Lichenification, late yaws and keratosis follicularis have the same effect. *M. Sydney Thomson.*

AMOEBIASIS AND DYSENTERY.

AMOEBIASIS.

TALAMONTI (Luigi). L'amebiasi in Migiurtinia. [**Amoebiasis in Migiurtinia.**—*Arch. Ital. Sci. Med. Colon.* 1934. Oct. 1. Vol. 15. No. 10. pp. 778–784. English summary (5 lines).

Migiurtinia is in the north-east of Italian Somaliland. Diarrhoea is common among the inhabitants. In two years August 1931–July 1933, sixty-two out of 197 deaths were registered as due to enterocolitis. The author, who was pathologist and Director at the Dante Hospital examined in 4½ months the stools of 900 persons, some suffering from diarrhoea but who had not had any treatment for it, others after a saline purge. He found *E. histolytica* in 409 or 45 per cent. He thinks there are three causes for this high incidence of infection: (1) the impure quality of the water—wells liable to contamination; (2) flies, present in enormous numbers during the monsoon period October to April; (3) personal contact between the healthy and those suffering from dysentery or passing the cysts of *E. histolytica* [as regards the risk of these last, see this *Bulletin*, Vol. 31, p. 734]. H. H. S.

KAWAI (T.), NAGAYOSHI (Y.) & KOO (C.). **A Survey of the Human Intestinal Protozoa in North Formosa.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. Aug. Vol. 33. No. 8 (353). [In Japanese. pp. 1149–1158. [34 refs.] English summary pp. 115–116.]

From the examination of a single stool specimen from 616 Chinese coolies and Japanese officials in Formosa the authors have found all the common intestinal protozoa with the exception of *Chilomastix mesnili*. Of *Entamoeba histolytica* there were 103 cases of which 96·12 per cent. gave no history of amoebiasis or other similar disease.

C. M. Wenyon.

KAN (Y.). **Results of Fecal Examination for Human Intestinal Protozoa in South Formosa.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. May. Vol. 33. No. 5 (350). [In Japanese pp. 823–831. [30 refs.] English summary pp. 87–88.]

At a small village, Hozan, in South Formosa the author examined for intestinal protozoa 40 Japanese marines and 156 Chinese school children. The Japanese showed an absence of *Entamoeba histolytica* and *Chilomastix mesnili* both of which were encountered amongst the children. Both groups showed *E. coli*, *E. bütschlii* and *E. nana* but an absence of trichomonas. C. M. W.

HIRAYAMA (Sigeki). Statistische Betrachtung und morphologische und biologische Studien ueber die parasitischen Amoeben des menschlichen Darmkanals. [**Intestinal Amoebae found in Kyusu, Japan.**—*Fukuoka-Ikwadaigaku-Zasshi (Fukuoka Acta Med.)*. 1934. Apr. Vol. 27. No. 4. [In Japanese. pp. 719–832. With 4 plates. [129 refs.] German summary pp. 35–37.]

A note on the examination for intestinal amoebae of 225 healthy and sick persons in the Kyûsû district of Japan. In 51·1 per cent. one (87)

or other of the 5 amoebae of man was found. *E. histolytica* was present in 6·7, *E. coli* in 18·7, *E. nana* in 36·9, *I. bütschlii* in 6·7, and *Dientamoeba fragilis* in 12. C. M. W.

HINSHAW (H. Corwin) & SHOWERS (Ethel M.). **A Survey of Human Intestinal Protozoan Parasites in Philadelphia.**—*Amer. Jl. Med. Sci.* 1934. July. Vol. 188. No. 1. pp. 108–116. [11 refs.]

The examination of 535 faecal specimens from 358 patients in the medical wards of a general hospital in Philadelphia during the winter of 1932–1933 revealed all the common intestinal protozoa of man. The highest incidence was 17·4 per cent. infected with *Endolimax nana* and the lowest 0·3 per cent. with *Dientamoeba fragilis*. *Entamoeba histolytica* occurred in 1·1 per cent. C. M. W.

ARNETT (John H.) & STABLER (R. M.). ***Entamoeba histolytica*: its Incidence in 1060 Philadelphia Students: its Morphological Characteristics.**—*Trans. College of Physicians of Philadelphia.* 1934. 4th Ser. Vol. 2. No. 2. pp. 181–182.

In the entire group were found—*Blastocystis* 63·2 per cent.; *E. coli* 14·5; *Endolimax nana* 11·4; *Giardia* 7·5; *Dientamoeba* 4·3; *Iodamoeba* 1·0; *Chilomastix* 0·94; *E. histolytica* 4·1 per cent.

H. M. Hanschell.

OWEN (William B.), HONESS (Ralph F.) & SIMON (James R.). **Protozoal Infestations of American Indian Children.**—*Jl. Amer. Med. Assoc.* 1934. Mar. 24. Vol. 102. No. 12. pp. 913–915. [11 refs.]

The examination of 83 North American Indian boys in Wyoming has revealed a very high incidence of intestinal protozoa. The results show that 93·9 per cent. were positive for one or more of the common forms. The percentage of infections were *E. coli* 68·6, *E. nana* 55·4, *I. bütschlii* 34·9, *E. histolytica* 26·5, *Giardia* 21·6, *Chilomastix* 2·4.

This high infection rate appeared to be definitely attributable to the very insanitary condition under which the boys live when they return to their homes from the Mission school at which they are resident.

C. M. W.

ANDREWS (Justin). **Incidence of Intestinal Protozoa with Special Reference to the Epidemiology of Amoebiasis in the Population of Fresnillo, Zacatecas, Mexico.**—*Amer. Jl. Hyg.* 1934. May. Vol. 19. No. 3. pp. 713–733. With 1 fig. [25 refs.]

During a survey of the inhabitants of Fresnillo, a small mining town situated 7,000 to 7,500 feet above sea level on a plateau in the State of Zacatecas, Mexico, the author found that of 2,302 inhabitants 76·9 per cent. were infected with one or more of the common intestinal protozoa. The native Mexicans were more commonly infected than the foreign residents, while of the latter those living in the vegetable garden district gave a higher incidence than others. As regards occupational groups the highest *E. histolytica* rate occurred amongst servants in foreign households, while of labourers those employed in the mines were more generally infected than those working above ground. It

appeared from an examination of the data collected that amoebic infection in foreign residents was derived primarily from the servants, who owed their high infection rate to the handling of raw vegetables which, according to local custom, had been subject to "freshening" with water which had every chance of being contaminated with human faeces. The infection incidence of the miners was due to the lack of satisfactory sanitary arrangements underground. The part played by the water supply, taken very largely from wells, was difficult to evaluate. It was clear, however, that during the rainy periods in summer there was opportunity for faecal material to be washed into the wells.

C. M. W.

SPECTOR (Bertha Kaplan) & BUKY (Florence).—**Viability of *Endamoeba histolytica* and *Endamoeba coli*. Effect of Drying.**—*Public Health Rep.* 1934. Mar. 23. Vol. 49. No. 12. pp. 379–385.

Employing the eosin test as an indication of viability, cysts staining with eosin being regarded as dead, the authors have found that cysts of *Entamoeba histolytica* or *E. coli* if smeared on the hands in faeces which are allowed to dry at room temperature die very rapidly. The number of cysts of *E. histolytica* to survive beyond 5 minutes was a very small proportion of those killed, while it was exceptional for any cyst to survive beyond 10 minutes. The fouling of the hands was intentionally far in excess of any that would be likely to occur under ordinary conditions.

C. M. W.

ANDREWS (Justin). **The Retention of *Endamoeba histolytica* Cysts under Finger-Nails.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 439–441.

This contribution is relevant to the question as to the part played by food handlers in the transmission of amoebiasis.

SPECTOR and BUKY'S (1934) experiments led them to state that in spite of conditions which "provided for a fouling of the hands far in excess of that which would be likely to occur under ordinary conditions, even with the most untidy or wilfully careless carrier . . . the number of cysts of *Endamoeba histolytica* to survive beyond five minutes was very small in proportion to those killed, and it was exceptional that any survived beyond ten minutes." The criterion of viability was alteration of cell wall permeability to a 1 : 1,000 aqueous solution of eosin. SPECTOR and BUKY'S work was thus a demonstration of the unlikelihood of faecal contamination of fingers of food handlers playing any part in transmitting amoebiasis.

Dr. Andrews devised and carried out experiments, here reported, to determine viability of amoebae lodged under the finger nails. His results show that cysts of *E. histolytica* survive under finger nails, as judged by debatable criterion of stainability with eosin, for much longer than five minutes; that there is less chance of this occurring with short well-manicured nails than with long closely applied not well-manicured nails; and that ordinary hand washing with soap and warm water generally suffices, especially with short nails, to dispose of faecal material which might have lodged under the nails.

The period of time during which the cysts fail to take stain is great enough to permit contamination of cold moist foods or beverages.

H. M. H.

FAUST (Ernest Carroll) & KAGY (Edwin S.). **Studies on the Pathology of Amebic Enteritis in Dogs.**—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 221-233. With 1 fig. [14 refs.]

The author describes three stages in the invasion by the amoeba of the gut of the untreated dog.

(1) Extensive superficial denudation of mucosa, similar to that in the kitten, except that the solitary lymph node in the dog is protected by epithelium and is not usually injured.

(2) Typical deep bottle-neck ulceration, unaccompanied by cellular infiltration.

(3) Chronic undermining ulceration, with superficial sloughing, frequently complicated by bacterial invasion.

The second and third types most nearly correspond to the human amoebic process.

In the dog, the caecum is the earliest site of amoebic attack ; but in more chronic cases the more evident, and often deeper, lesions are found in lower colon and rectum. The earliest superficial tissue changes, as well as the typical bottle neck ulcers, and the honeycombing destruction of submucosa, all indicate that lytic action is most important in development of the amoebic process, although mechanical action aids the amoebae in their penetration and migration. While bacteria, accompanying or following the amoebae, complicate the picture, there is adequate evidence that the amoebae alone are responsible for the typical lesion. Amoebae in uncomplicated cases provoke no polymorphonuclear leucocyte infiltration, but monocytes may invade the damaged area. The amoebae do not appreciably stimulate the solitary lymph nodes. Where bacteria accompany or follow the amoebae, there is profound leucocytic infiltration and lymph node response.

H. M. H.

MELENEY (Henry E.) & FRYE (William W.). **Studies of *Endamoeba histolytica* and Other Intestinal Protozoa in Tennessee. VII. The Histopathology of Intestinal Amoebiasis in the Kitten and in Man.**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 84-105. With 6 figs. [10 refs.]

This paper describes fully and illustrates the histological picture of amoebic infection of the colon as disclosed by examination of tissue from 120 kittens, and three human autopsies, performed shortly after death.

In the kittens, massive dilatation of submucosal lymph vessels containing necrotic debris, bacteria, and amoebae, was frequently found. Those autopsied several hours after death, and others at known intervals after death, showed only an occasional slight advance of amoebae into the unaltered tissues beyond the lesions.

The three human autopsies showed all types of amoebic lesions, from shallow mucosal lesions to deep abscesses of submucosa. As compared with the kitten lesions, the human showed greater loss of epithelium in the bases of glands without necrosis of stroma or mucosa ; (2) less massive coagulation of mucosa ; (3) more undermining of mucosa by necrotic lesions in submucosa ; (4) extensive migration of amoebae into normal tissue, and the authors believe this migration to be primarily ante-mortem.

H. M. H.

LEIVA (Lamberto). **A Fatal Case of Nondysenteric Amoebiasis.**—*Philippine Jl. Sci.* 1934. Feb. Vol. 53. No. 2. pp. 159–167. With 3 plates. [10 refs.]

Necropsy revealed abscess of the liver, lung, kidney, and brain. The intestines were normal, with no scars or ulcers, except in the caecum where “minute pinhead erosions” were visible, and smears from them revealed, microscopically, trophozoites and cysts of *E. histolytica*. In the walls of the abscesses in liver, lung, kidney, and brain, trophozoites of *E. histolytica* were demonstrated. H. M. H.

GIORDANO (Mario). Contributo alla terapia dell’amebiasi intestinale. [**The Treatment of Intestinal Amoebiasis.**]—*Arch. Ital. Sci. Med. Colon.* 1934. Sept. 1. Vol. 15. No. 9. pp. 706–720. English summary (5 lines).

The author records 30 cases of amoebic dysentery, that is, all were passing blood and mucus and in most of them the entamoeba was seen. Thirteen had previously been treated by emetine (some had had more than one course), stovarsol, or yatren without cure. They were then given Vioform (Iodo-oxyquinoline hydrochloride) Ciba, by mouth in doses of 0.75 gm. daily for 10 days, the course being repeated after an interval of 5–7 days. In no instance were any toxic symptoms produced, and the entamoebae disappeared. In two patients they were found again later, but both of these lived in unhygienic surroundings with every chance of reinfection. H. H. S.

FAUST (Ernest Carroll) & KAGY (Edwin S.). **Studies on the Effect of feeding Ventriculin, Liver Extract and Raw Liver to Dogs Experimentally Infected with *Endamoeba histolytica*.**—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 235–255. With 1 fig.

Following on preliminary observations of the benefit of feeding raw liver to dogs infected with *E. histolytica* the authors undertook the further experiments here recorded.

The results of the experiments demonstrated that ventriculin was consistently harmful to the host, it did not check invasion of amoebae and it did reduce resistance of gut wall to bacterial invasion. Liver extract was beneficial to the host and appreciably arrested the amoebic process. Raw liver not only helped in arresting the amoebic process, but in some cases produced complete eradication of amoebae. Evidence gathered from these experiments suggests that efficacy of liver feedings consists not in stimulating haematopoietic organs, but by direct contact with tissues attacked by the amoebae. It is not amoebicidal but amoebostatic. Furthermore, the neutralizing effect of liver on histamin and other degeneration products of proteins in the bowel lumen, conceivably aids the healing process and reduces danger of bacterial invasion. H. M. H.

HOGUE (M. J.). **Further Studies on the Effect of Amoebicidal Drugs on Tissue Culture Cells (Arsenious Trithio Salicylic Acid, Carbarsone, Kurehl Bismuth Iodide, Proparsamide, Vioform).**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 443–456. With 6 figs.

The tissue cultures were of 8-day old chick embryo intestines (Locke-Lewis medium). The five drugs were found to affect the tissues differently. A.T.S. acid was very toxic to all the tissues grown *in vitro*. Carbarsone was not very injurious to tissues of digestive tract,

though epithelium was sometimes affected. Kurchi bismuth iodide in low dilutions kills all the tissue culture cells; in higher dilutions it is injurious to fibroblasts but not to epithelium. Proparsamide is very injurious to sympathetic nerves and has little effect on other tissues. Vioform was very toxic to fibroblasts in all the dilutions tried, but the epithelial cells survived in its higher dilutions. Of the three arsenic compounds, carbarsone (28.85 per cent. arsenic content, valency 5) was least injurious to the tissue culture cells; proparsamide (26 per cent. As. valency 5) affected only the nerves; A.T.S. (13 per cent. As. valency 3) was the most injurious to all the cells. *H. M. H.*

DESCHIENS (R.). Influence du froid sur les formes végétatives de l'amibe dysentérique. [**Influence of Cold on the Vegetative Forms of *E. histolytica*.**—*C. R. Soc. Biol.* 1934. Vol. 115. No. 8. pp. 793-795.]

—. Méthode de culture, à des températures alternées, de l'amibe dysentérique. [**Cultivation of *E. histolytica* at Alternated Temperatures.**—*Ibid.* No. 10. pp. 1072-1073.]

Working with *Entamoeba histolytica* in cultures the author has found that the survival of the amoeba, as tested by subculture into fresh medium, increases with a fall in temperature. Thus, at 28°C. the survival was 5 days, at 18°C. 9 days and at 5°C. 11 days. The removal every 48 hours of the liquid portion of the medium and its replacement by liquid from fresh tubes increased the survival at 25°C. from 5 to 8 days. At 0°C. the time was only 56 hours.

In the second paper an account is given of a prolongation of the survival time by alternate exposure of the cultures to high and low temperatures. Thus, a culture after 48 hours incubation at 37°C. was exposed to 3°C. for 3 days, followed by 1 day at 37°C. and then again by 3 days at 3°C. and so on. The amoebae were still alive at the 18th or 19th day. *C. M. Wenyon.*

DESCHIENS (R.). Culture et enkystement de l'amibe dysentérique dans les eaux d'égout. [**Growth and Encystment of *E. histolytica* in Drainage Water.**—*C. R. Soc. Biol.* 1934. Vol. 115. No. 7. pp. 701-704.]

Experimenting with the possibility of cultivating *Entamoeba histolytica* in ordinary water the author has found that in certain cases, as, for instance, when the water has been enriched with material draining from slaughter houses, growth is possible if the temperature reaches a sufficiently high degree, as it may do in the tropics. Moreover under such conditions encystment of the amoeba may take place, for the author has found that this can be brought about by the addition of horse serum to the medium. It would seem possible, therefore, that in nature unencysted amoebae escaping from the intestine may survive and multiply for a while if they gain access to suitable water and finally encyst. *C. M. W.*

TSUCHIYA (H.). Further Studies on the Cultivation of *Endamoeba histolytica* and a Complement Fixation Test for Amebiasis.—*Jl. Lab. & Clin. Med.* 1934. Feb. Vol. 19. No. 5. pp. 495-504. [30 refs.]

For the cultivation of *E. histolytica* the author advocates the use of a broth to which is added for each test tube (8 cc. of broth) two 4 mm.

loopfuls of a sterile mixture of rice starch and animal charcoal in the proportion of 2 : 1. If this medium is inoculated with washed cysts of the amoeba a good growth is obtained. Sub-cultures are made every 48 hours either into the liquid medium alone or into the medium on the surface of a Dorsett's egg slant. It is claimed that other intestinal amoebae will not grow by this method. With amoebae thus cultivated an antigen was prepared by Craig's method. Of 153 persons whose sera were tested, 135 known to be free from amoebic infection gave a negative complement fixation test. Of the remainder 8 known carriers of *E. histolytica*, 5 cases diagnosed as clinical amoebic dysentery and 4 cases of ulcerative colitis without amoebae were positive, while 1 case of clinical amoebic dysentery was negative. C. M. W.

PAVLOFF (P.). Recherches sur la présence de kystes à quatre noyaux d'amibes dysentériques dans les selles des porcelets. (Note préliminaire.) [**Four-nucleated Cysts of the Dysentery Amoeba in the Faeces of Young Pigs.**]*Ann. Parasit. Humaine et Comparée.* 1934. Sept. 1. Vol. 12. No. 5. pp. 394-395.

The paper records merely a negative result, namely the failure to discover four-nucleated cysts of the type of those of the dysentery amoeba in young pigs in France after more than 500 examinations. The examination was undertaken in view of KESSEL's statement that in China 30 per cent. of young pigs examined by him revealed such cysts. C. M. W.

BACILLARY DYSENTERY.

FEEMSTER (Roy F.). **Use of Bacteriophage in Diagnosis of Bacillary Dysentery.**—*Jl. Infect. Dis.* 1934. Sept.-Oct. Vol. 55. No. 2. pp. 190-194.

This is an interesting contribution to the laboratory diagnosis of dysentery. It is comparatively rare to be able to isolate the causative dysentery bacillus from a stool which has been sent to a laboratory. This was formerly ascribed to the small number of organisms present in mild cases and to their overgrowth by other bacteria. We have now to add another cause for the sterility of platings—the fact that, by the time the stool comes under examination, phage with its lytic and inhibitory action has made its appearance. "A stool sample . . . usually contains both the bacillus and the bacteriophage, and during the interval between the collection of the sample and its arrival at the laboratory the organisms are killed." The author has utilized an institutional outbreak of dysentery, of more than 100 cases and 18 deaths in a population of 1,750, to apply the dysentery phage test as a diagnostic procedure in addition to culture and serum-agglutination. The bacillus, of Y-Hiss type, was isolated only six times out of 90 stool examinations. Agglutination tests with stock cultures were positive in 36 out of 55 patients for blood samples taken 5 to 36 days after the onset of illness, while 17 patients out of 18 gave agglutination at 1-40, six months after the epidemic, with the culture isolated and still higher titres with stock cultures. The phage tests, which form the main subjects of this article, gave 29 positive determinations out of 81 stool examinations against the 6 out of 90 for bacillus culture. A very interesting table gives the positive results in this phage test week by week. It shows this to have been for the 1st, 2nd, 3rd and 4th week

2 out of 6, 8 out of 10, 5 out of 11, and 2 out of 14. Six months after the epidemic the phage had disappeared from the stools. The technique is as follows :—

(1) Cover 1 to 2 gm. faeces with 10–20 cc. nutrient broth. (2) Allow to remain in contact 30 min. or longer to allow phage to diffuse. (3) Decant the broth carefully and filter through a Berkefeld candle. (4) Place 0.5 cc. filtrate and 0.05 cc. 18-hr. broth culture of the causal organism in a tube of broth. (5) Set up a control tube with no filtrate. (6) Examine tubes after 24, 48 and 72 hrs. for clearing by phage action. (7) Test any doubtful tubes by the method of plating out with a 24-hr. broth culture to obtain plaques.

Of course, in cases where the causal organism has not been isolated, it will be necessary to set up the filtrate against a number of organisms of the dysentery group or, if the disease is not clinically dysentery, with other organisms, such as those of the Salmonella group. "The length of the series will depend on the clinical picture." [The specificity of the phage does not seem to have been actually investigated.]

W. F. Harvey.

MCCLEAN (S. D.) & MARSH (Frank). **Bacillary Dysentery due to Flexner, Type "Z" presenting Some Unusual Features.**—*Lancet*. 1934. Sept. 8. pp. 545–546.

The authors describe a case of dysentery in which "at no time was the classic picture of blood, pus, mucus and epithelial cells presented by the stools." The stool was consistently diarrhoeic. Dysentery bacilli of "Z" type were easily isolated and gave characteristic agglutination with Medical Research Council standard sera, while the patient's serum also gave typical agglutination of standard agglutinable type culture "Z." It is thought that the absence of mucus in the stools may have accounted for the ease of isolation of the causal bacterium.

W. F. Harvey.

REID (P. E.), ANDERSON (M. X.), STUBBLEFIELD (H. I.) & IVY (A. C.). **Protective Action of Sodium Thiocyanate against Dysentery Toxin (Shiga). An Experimental Study in Dogs and Rabbits.**—*Jl. Infect. Dis.* 1934. July–Aug. Vol. 55. No. 1. pp. 112–122.

It was discovered by accident that a 4 to 5 weeks previous injection of sodium thiocyanate in dogs appeared to protect them against lethal doses of the toxic filtrate from a Shiga dysentery culture. The matter was investigated further and it was found that there was a definite protection to dogs afforded by 60 mgm. sodium thiocyanate orally or 20 mgm. intravenously. This protection, however, was not manifest in rabbits. Now it is known that sodium thiocyanate itself is relatively non-toxic, but that it is only slowly eliminated and therefore tends to accumulate when it is administered continuously. A mechanism for the action of the thiocyanate has been sought in the claim that it tends to prevent coagulation of proteins or to render them more "soluble." Some such preventive action may come into play to protect the colloidal cytoplasm of cells from the dysentery toxin. The authors, however, prefer to offer no explanation of the action, but they suggest the possibility of thiocyanate as a therapeutic agent in human Shiga dysentery. It "may prove to be effective prophylactically" . . . may also be of benefit if given early in the disease," but is not likely to be of

use "if given during collapse or after extensive bloody diarrhoea." The dosage suggested is, "as a prophylactic measure . . . the daily oral administration of 20 mgm. . . . per kilogram . . . of body weight in broken doses for three days. . . . This should afford protection against a lethal dose of dysentery toxin for at least a month."

W. F. Harvey.

MURASHIMA (Tetsuo). Instances corroborating the Efficacy of Oral Vaccination against Dysentery and Yekiri.—*Jl. Public Health Assoc. Japan.* 1934 July. Vol. 10. No. 7. pp. 1-7.

[Many of the statistics presented as showing efficacy of a prophylactic vaccine are not comparable in respect of the vaccinated and the non-vaccinated. The totals of the non-vaccinated who are "at risk" are not accurately known and in an epidemic the vaccine is often given after the disease has made its appearance and already taken its toll of susceptible individuals who may even be reckoned among the non-vaccinated.] In the instance given here the vaccine was administered some two months before a real water-borne and explosive epidemic of dysentery broke out. The vaccine was given orally, in tablet form and contained three strains of dysentery bacilli in equal portions. One of these strains seems to have been the causative organism in the epidemic, which in the course of 12 days attacked 39 households out of 65, 90 persons out of the entire population of 316, and 45 children of ages 2 to 14 years out of 95. Of the 45 children attacked 10 out of a total of 30 were vaccinated (33·3 per cent.) and 35 out of 65 were non-vaccinated (53·8 per cent.). The mortality figures were 1 out of 10 for the vaccinated and 5 out of 35 for the unvaccinated.

W. F. Harvey.

MIXED AND UNCLASSED DYSENTERY.

- LARGE (D. T. M.). Dysentery among Troops in Quetta. Part I and Part II A ; B ; C.**—*Jl. Roy. Army Med. Corps.* 1934. Aug. & Sept. Vol. 63. Nos. 2 & 3. pp. 80-92. With 1 chart ; 157-167. With 1 chart. [9 refs.]
- & **SANKARAN (O. K.). Dysentery among Troops in Quetta. Part II D ; E.**—*Ibid.* Oct. & Nov. Nos. 4 & 5. pp. 231-237. [4 refs] ; 303-312. [3 refs.]

An epidemiological and laboratory case-survey.

During 1932 and 1933, the number of cases examined in the laboratory was 1,536, of which 63 per cent. were bacillary, the remainder amoebic (166 cases *E. histolytica*), or of indefinite nature. A dysentery bacillus was isolated in 70 per cent. of the bacillary cases, the other 30 per cent. were classed on microscopic examination of the exudate. Of the cases showing a dysentery bacillus, Flexner group accounted for 63·5 per cent. ; Sonne 14·0 ; Shiga 10·4 ; para Shiga 3·0 ; Schmitz 5·6 ; para Schmitz 2·0.

Dysentery in Quetta is characterized by two annual increases, May-June, and August-September, with a marked lull in July, the increases preceded by a period during which potentially irritant particles of silica are washed in excess into the water supply by rain ; and frequent dust-raising winds occur.

The usual close relationship between humidity and flies, and flies and dysentery exists. Infection of troops probably also occurred through the medium of missed cases who had contracted infection in the insanitary and fly infested bazaar ; and also of missed cases among children and Indian servants.

Bact. dysenteriae Sonne was prevalent in the spring months only, *Bact. dysenteriae* Shiga in the autumn. The better known types of Flexner bacilli are scarce in spring but predominate in autumn. This may have a bearing on vaccine prophylaxis of dysentery. *H. M. H.*

WEINBERGER (Herbert L.). **Dysentery. Report of Three Cases in One Family due to Atypical *Bacillus dysenteriae* and *Endamoeba histolytica*.**—*Jl. Amer. Med. Assoc.* 1934. Mar. 24. Vol. 102. No. 12. pp. 916-917.

These three cases were all associated with high fever, leucocytosis, prostration, and signs and symptoms of an acute condition of the abdomen. This is unusual in amoebiasis alone, and is probably due to an associated infection with one or other of the bacillary dysentery group. This proved to be true. In all three cases *Bact. dysenteriae* (Schorer and Duval 1904) was isolated 60 days before discovery of *E. histolytica*. Combination treatment by emetine and chiniofon proved effective against the amoebiasis. *H. M. H.*

BONNE (W. M.). Rivanol bij dysenterie. [**Rivanol in Dysentery.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Aug. 14. Vol. 74. No. 17. pp. 1065-1080. English summary.

Parallel series of cases were treated, the one with the ordinary medicaments and the other with rivanol. This was done for both amoebic and bacillary dysentery.

In the series of amoebic dysentery patients, in which characteristic motile amoebae carrying erythrocytes were found, twenty were treated with magnesium sulphate on the first day followed by 50 mgm. rivanol three times a day, while another twenty were treated from their first day for 5 days with 30 mgm. emetine and 1 gm. yatren three times a day by deep subcutaneous injection and *per os* respectively. These cases are compared for a variety of characters. In both, blood and mucus disappeared from the stools by the 6th day with 7 exceptions in the case of rivanol and 3 in the case of emetine-yatren. The general condition of the patient treated with rivanol sometimes gave rise to anxiety on the 6th day but not so with emetine-yatren. After the use of emetine-yatren erythrocyte-containing amoebae were never found in the stools on the 5th or 6th day, whilst for these days with rivanol 9 cases still showed amoebae. In the rivanol series one fatal case occurred. The conclusion is drawn that rivanol is unsuitable for amoebic dysentery in the doses used.

A further series was investigated of cases of bacillary dysentery type Y, and dysentery without known cause. They were all cases with blood and mucus in the stools and no amoebae. Series I contained 5 cases treated with bismuth and opium and 25 cases with yatren preceded by a laxative dose of magnesium sulphate. Series II, of 30 cases, were treated with rivanol preceded by magnesium sulphate and series III, also of 30 cases, were treated with magnesium sulphate only.

It was found that the treatment with magnesium sulphate alone gave quite satisfactory results and that these were less satisfactory with rivanol. The treatment with yatren, 1 gm. three times daily by the mouth, gave the best results.

W. F. Harvey.

BYCHOWSKY (Arieh). *Lamblia and Trichomonas Enteritis and its Relation to Amoebic Dysentery.*—*Jl. Egyptian Med. Assoc.* 1933. Dec. Vol. 16. No. 12. pp. 1132-1141. [11 refs.]

Though flagellate infections of the intestine are very common in Egypt in persons suffering from various forms of enteritis, there is little evidence that they are actually pathogenic, for a careful examination will nearly always reveal an amoebic infection to account for the symptoms present.

C. M. Wenyon.

LAUDA (E.). Zur Therapie der Lamblienenteritis. [**Treatment of Lamblial Enteritis.**]—*Wien. Klin. Woch.* 1934. Sept. 21. Vol. 47. No. 38. pp. 1132-1133.

A patient 33 years of age with symptoms of enterocolitis was found to have a very heavy lamblia infection. By duodenal sound 0.3 gm. of neosalvarsan in 200 cc. of water was introduced into the duodenum. The diarrhoea immediately ceased and by the third day no lamblia could be found in the stools. The patient seemed to have recovered, nevertheless the parasites reappeared in spite of treatment with spirocid. The treatment was repeated. It again brought about the disappearance of the parasites which this time did not reappear. The author argues in favour of the pathogenicity of this flagellate. C. M. W.

GROSS (M.). Die Lamblia im Kindesalter. [**Giardiasis in Children.**]—*Schweiz. Med. Woch.* 1934. June 16. No. 24. pp. 551-554.

Writing of lamblia infections in children in Bern the author takes it for granted that the flagellate is pathogenic and ascribes to it the various symptoms which his cases exhibited—chronic diarrhoea, loss of appetite and the troubles consequent on these. Treatment was carried out by injections of myosalvarsan (sulfarsenol) as in syphilis or better by oral administration of spirocid (stovarsol). Rapid improvement with disappearance of parasites from the stools followed and if relapse occurred the illness was not so severe as it had been in the first instance.

C. M. W.

LIDDO (Salvatore). Anomalie delle cisti di "*Lamblia intestinalis*." [**Anomalies of Cysts of *G. intestinalis*.**]—*Pathologica.* 1934. Sept. 15. Vol. 26. No. 515. pp. 607-608. English summary (4 lines).

In a case of lamblia infection the author has seen abnormally large cysts up to 17.5 μ in length. He thinks it possible that man may harbour more than one species of this flagellate.

C. M. W.

ANDERSON (Hamilton H.) & REED (Alfred C.). Carbarsone Rectally in Amebiasis.—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 257-267.

ANDERSON (Hamilton H.) & REED (Alfred C.). Untoward Effects of Anti-Amebic Drugs.—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 269-281. With 1 fig. [16 refs.]

- AZMY (Soliman) & TAHA (S.). The Treatment of Amoebiasis by Iodo-Chlor-Hydroxyl-Quinoline (Empero-Vioform).—*Jl. Egyptian Med. Assoc.* 1934. Oct. Vol. 17. No. 10. pp. 809-814.
- BONNE (W. M.). Bacillaire dysenterie type Y.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. July 31. Vol. 74. No. 16. pp. 982-996. With 2 charts & 6 figs. on 2 plates. English summary.
- CALLENDER (G. R.). The Differential Pathology of Dysentery.—*Amer. Jl. Trop. Med.* 1934. May. Vol. 14. No. 3. pp. 207-220. With 4 figs.
- CASTEX (M. R.) & GREENWAY (Daniel). Influencia del tratamiento específico, sobre una cepa de *Entamoeba histolytica*.—Reprinted from *Bol. Acad. Nac. Med. Buenos Aires.* 1930. Nov. 21. 8 pp. With 8 figs.
- CASTEX (Mariano R.) & GREENWAY (Daniel). Consideraciones parasitológicas y clínicas sobre 2700 casos de amebiasis intestinal.—*Prensa Méd. Argentina.* 1934. Oct. 31. Vol. 21. No. 44. pp. 2049-2070. With 2 maps. [122 refs.]
- CHANG (C.) & ROBERTSON (D. S.). Amoebic Liver Abscess in Manchuria with Special Reference to Intraperitoneal Rupture.—*Chinese Med. Jl.* 1934. Apr. Vol. 48. No. 4. pp. 375-380. [10 refs.]
- CHOPRA (R. N.). The Toxic Effects of Emetine.—*Indian Med. Gaz.* 1934. June. Vol. 69. No. 6. pp. 309-312.
- CHOPRA (R. N.) & SEN (S.). Carbarsone in Intestinal Amoebiasis. Part II.—*Indian Med. Gaz.* 1934. July. Vol. 69. No. 7. pp. 375-380.
- CRAIG (Charles F.). Clinical Aspects of Amebiasis.—*New Orleans Med. & Surg. Jl.* 1934. Mar. Vol. 86. No. 8. pp. 609-613.
- CRAIG (Charles F.). The Epidemiology of Amebiasis. Clinical Lecture at Cleveland Session.—*Jl. Amer. Med. Assoc.* 1934. Oct. 6. Vol. 103. No. 14. pp. 1061-1063.
- CREAGH (E. P. N.). Report on a Case of Hepatic Abscess with Spontaneous Evacuation through the Right Lung and Bronchial Tree.—*Jl. Roy. Army Med. Corps.* 1934. Sept. Vol. 63. No. 3. pp. 186-190. With 2 figs. & 1 chart.
- DUVAL (Charles W.). Etiology and Pathology of Bacillary Dysentery.—*New Orleans Med. & Surg. Jl.* 1934. Mar. Vol. 86. No. 8. pp. 599-601.
- EARNSHAW (P. A.). The Raw Apple Diet in the Treatment of Dysentery.—*Med. Jl. Australia.* 1934. Sept. 8. 21st Year. Vol. 2. No. 10. pp. 305-310. [16 refs.]
- FAUST (Ernest Carroll). The Distribution and Diagnosis of Amebic Enteritis in the Southern United States.—*New Orleans Med. & Surg. Jl.* 1934. Mar. Vol. 86. No. 9. pp. 605-609. [39 refs.]
- FRADKIN (William Z.). A Simple Sigmoidoscopic Aspirator.—*Jl. Amer. Med. Assoc.* 1934. July 7. Vol. 103. No. 1. p. 21. With 1 fig.
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BLACKWATER FEVER.

- i. STEPHENS (J. W. W.). **The Distribution of Blackwater Fever (Summary).**—*Ann. Trop. Med. & Parasit.* 1934. Mar. 29. Vol. 28. No. 1. pp. 37–40.
- ii. ——. **The Distribution of Blackwater Fever in Central America, South America and the West Indies.**—*Ibid.* 1933. July 7. Vol. 27. No. 2. pp. 283–307. With 2 maps. [3 pages of refs.]

i. Stephens gives here a brief summary of his seven previous papers on the distribution of blackwater fever. He considers that it is impossible to give any comparative figures indicating the frequency of the disease in the countries and localities named. He has, however, marked with an asterisk those places where blackwater fever is not an unusual condition. It is impossible to give an adequate summary of this short and valuable paper which itself is a very brief summary of the result of the author's prolonged researches on the geographical distribution of blackwater fever. It must be consulted in the original by those interested.

ii. This paper consists entirely of a series of tables giving details of the distribution of blackwater in the areas mentioned in the title, and must be consulted in the original by those interested. *W. Yorke.*

- i. NAUMANN (H. E.). *Betrachtungen zum Schwarzwasserfieber. [Meditations in Blackwater Fever.]*—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. June. Vol. 37. No. 6. pp. 299–307.
- ii. ——. *Schluss zu "Betrachtungen zum Schwarzwasserfieber."* (Aus: *Arch. Schiffs- u. Tropenhyg.*, Bd. 37, S.299.)—*Ibid.* 1934. Apr. Vol. 38. No. 4. pp. 171–174.

i. The author believes that two important factors in the genesis of blackwater fever are malaria and liver damage.

In support of his second contention he lays stress on the fact that blackwater fever is rarely seen in young children.* He points out that children suffering from malaria are not brought for treatment until they have had fever for some time, and that when so brought they are slightly icteric, very anaemic and vomiting frequently; nevertheless, such children respond quickly to quinine treatment and do not develop blackwater fever. It follows that neither malaria nor destruction of red corpuscles suffices to explain the onset of blackwater; there must be another factor.

With the object of discovering what this is the author has made a careful study of the history and clinical findings disclosed by his cases of blackwater fever. Details are given of a series of 15 cases in Haiti. He lays particular stress on the history of Case 11. The patient was a young man, aged 27, who in 1929–1930 was treated by the author for severe tropical malaria. He recovered completely and since had had no fever and had taken no prophylactic measure. Owing to the depressed condition of trade he could not find enough work to occupy him and sought solace for some months in drinking a bottle of rum nightly. This resulted in severe liver trouble. He then developed malaria and

*This is not the experience of GIGLIOLI who on the Demerara River found children to be three times as liable to blackwater as adults. Twenty-four cases out of 63 were in children under ten years [*Trans. Roy. Soc. Trop. Med. & Hyg.* 1932. Vol. 26. p. 204.]

the liver was found to be greatly enlarged. The malaria was treated with plasmochin compound and blackwater supervened. Ultimately the patient recovered. The author comments on the fact that the first attack of malaria was readily cured without mishap, but that the next attack which occurred after alcohol excesses resulted in blackwater. The patient, after his attack of blackwater, gave up alcohol, and although some months later he had another attack of malaria this was dealt with satisfactorily without any trace of blackwater.

As a result of analysis of his cases Naumann believes that blackwater fever occurs in malaria patients in whom the liver is damaged ; and that the two chief causes of this are stasis and alcoholic abuse.

In an addendum details are given of two malaria patients who developed blackwater although the only treatment they received was a mixture of atebirin and plasmochin.

ii. In this paper the author considers the question of the proper treatment of blackwater fever. He recalls that the main cause of death in the fatal cases of the series described in his previous paper was heart failure following anaemia. [Four of the 15 cases ended fatally.] He asks whether it is possible to prevent or anticipate the destruction of red cells, or whether it is possible to cause a quick regeneration of red cells, thus mitigating the evil consequences of the anaemia. In view of the results obtained by the author with campolon in paroxysmal haemoglobinuria, it was decided to give this drug a trial in blackwater fever. The exact treatment given to a patient was as follows :—

The malaria was treated with 0.1 gm. of atebirin and 0.02 gm. of plasmochin twice or thrice daily ; (the author remarks that he prefers atebirin alone at first as it upsets the stomach less than plasmochin) ; glucose and insulin ; and campolon 1 to 2 ampoules daily. The results were excellent ; the urine cleared by the fourth day and the blood haemoglobin had risen from 23 per cent. to 65 per cent. after 10 injections of campolon.

The question then arose whether this good result was due to atebirin or to campolon. Shortly afterwards an epidemic of malaria occurred and during this 41 cases developed blackwater fever. Of these, 18 were treated as above and all did well ; the remaining 23 were treated by other doctors and 7 died. In all the blackwater cases malaria parasites were found. In this great epidemic of malaria it was common to find 4 to 7 cases in one family and yet only one of these would develop blackwater fever. Naumann, as the result of his enquiries into this matter, reached the general conclusion that all the robust individuals escaped blackwater and that this disease only occurred amongst those of feeble constitution.

The author's 18 cases of blackwater either came to him with the disease or it developed within 3 days of their coming to him for malaria. The only treatment given was atebirin. It follows, therefore, that atebirin does not prevent the development of blackwater ; nevertheless, in the author's opinion, it is the best drug to use in blackwater, because, of the malaria remedies, it has the least damaging effect on the red cells and the whole organism.

Therapy to support liver function is important, so as to render the liver capable of dealing with the enormous number of destroyed red cells and of converting the haemoglobin into bile, thereby saving the kidneys and preventing suppression of urine through blocking of the uriniferous tubules. The part played by campolon is that it causes

quick regeneration of the red blood corpuscles and also stimulates the whole organism.*

W. Y.

HALL (G. Rome). **Comments on Blackwater Fever, and a Group of Special Cases.**—*Jl. Trop. Med. & Hyg.* 1934. Feb. 1. Vol. 37. No. 3. pp. 33–36.

Very brief details are given concerning a group of blackwater cases which occurred at the Bibiani Mine, Gold Coast. With the exception of one patient they were all working in the Extractor House, where the last stages of the extraction of gold takes place. The great bulk of the paper is highly speculative and should be consulted by those interested in the original, as the reviewer is unable to make anything of it. In fact, there seems little evidence that many of the cases which occurred amongst the native staff were really blackwater. It may be of significance that it is stated that each of these patients suffered from haematuria, but, on the other hand, it may equally well be of no significance beyond the fact that the author fails to distinguish this from haemoglobinuria.†

W. Y.

AMY (A. C.). **Haemoglobinuria: a New Problem on the Indian Frontier.**—*Jl. Roy. Army Med. Corps.* 1934. Mar., Apr., May. Vol. 62. Nos. 3, 4 & 5. pp. 178–191; 269–278; 318–329. [48 refs.]

These papers deal with a recent and hitherto unknown phenomenon on the Indian frontier, viz., haemoglobinuria in some way associated with malaria and confined to Indian troops and followers. So far there are records of 10 cases with 6 deaths.

The geographical distribution of the cases is limited to the frontier and the stations in which they occurred are mentioned. Up to date, no case of blackwater fever in India has been reported west of longitude 75° (Amritsar). The nearest point to that in the present series is longitude 71·5° (Kohat), which is 250 miles from Amritsar. The author, moreover, emphasizes that the Punjab is not recognized as a blackwater fever area. Five of the present series of cases were isolated, and five—in Quetta—were grouped both as regards time and place.

Details are given regarding the race, caste, age and occupation of the patients. It is stated that the fact that all the patients were Indians "is dead against a blackwater fever hypothesis." Malignant tertian parasites were found in four cases, simple tertian in five, and no parasites in one case.

The author next proceeds to consider what he calls "the burning question in this series of cases." Prior to the development of haemoglobinuria, the total amounts of quinine taken were :—

*Campolon (a Bayer product) is described as "a specially fractionated extract of liver of high therapeutic potency." It is given intramuscularly, 2 cc. equalling 500 gm. of fresh liver by mouth.—ED.

†The author states that AsH₃ was possibly present in the fumes in the final stage of gold extraction. Among the symptoms of AsH₃ poisoning mentioned by LEGGE ("Industrial Maladies." 1934. Oxford. Med. Publ. p. 90) are vomiting, jaundice, and haemoglobinuria or haematuria with strangury.—ED.

1 patient 32 grains spread evenly over 3½ days (followed by atebtrin)

1 " 50 " " " 2½ "

2 patients 90 " " " 3 "

1 patient 90 " " " 4½ "

1 " 110 " " " 5½ "

1 " 120 " " " 6 "

Three patients had taken no quinine; two of them died and in one the disease was very mild.

Prior to the onset of haemoglobinuria the amounts of atebtrin taken were :—

1 patient 1.5 gm., spread evenly over 5 days.

1 " 1.8 " " " 6 "

1 " 2.1 " " " 7 "

1 " 1.2 " " " 4 " (preceded by quinine)

Prior to the onset of haemoglobinuria the amounts of plasmoquine taken were :—

4 patients 0.06 gm., spread evenly over 2 days.

1 patient 0.06 " " " 3 "

1 " 0.08 " " " 2 "

1 " 0.09 " " " 4½ "

1 " 0.10 " " " 3½ "

1 " 0.13 " " " 4½ "

1 " 0.18 " " " 6 "

Before the attack of haemoglobinuria set in, 6 patients therefore were on quinine, 3 on atebtrin, 1 on quinine followed by atebtrin, and all of them received plasmoquine. Attention is drawn to the comparatively small doses (daily and total) of each of these drugs. The author adds, however, "It is reasonably certain that some of the patients may have suffered from plasmoquine toxicity." He quotes from the literature to the effect that whereas quinine cannot safely be given to cases of blackwater fever because of the danger of producing further haemolysis, plasmoquine can be safely used at any stage of the disease. A summary of the signs of plasmoquine poisoning is given in this *Bulletin*, Vol. 30, pp. 195-6, and Amy draws attention to the close resemblance between this condition and blackwater fever. As regards plasmoquine dosage, SINTON states that doses as high as 0.2 and 0.32 gm. daily have been given, and FLETCHER quotes 0.18 gm. as not infrequent and 0.1 gm. as common. In contrast it is emphasized that in the present series the greatest amount taken was 0.18 gm. and that this was spread over 6 days. Judging from the literature it would seem that a daily dose of 0.03 gm. of plasmoquine is reasonably safe, but that even this small dose has been known to produce haemoglobinuria. Up to August, 1933, the standard dose throughout the army in India was 0.03 gm. daily; in the case of British troops mild toxicity was occasionally noticed, but severe poisoning has never been reported. There is some evidence that plasmoquine has a cumulative effect. In the case of Indian troops, and as a direct result of the Quetta cases of haemoglobinuria, the standard dose has been halved since August, 1933, and no further instances of haemoglobinuria have been reported.

In the second paper the author considers some of the points in which his series of cases so strikingly resemble blackwater fever. Having briefly summarized the chief features of blackwater fever he passes to a consideration of the manifestations of plasmoquine poisoning. These are practically speaking indistinguishable except that :—(1) Oxyhaemoglobinaemia, with oxyhaemoglobinuria, is never a result

of plasmoquine poisoning, but does occur in blackwater; and (2) so-called cyanosis is a feature of poisoning, but is not met with in blackwater fever.

Amy writes :—

"When it is noted that a patient is suffering from oxyhaemoglobinuria, and that cyanosis is not present, it is clear that—in the present state of our knowledge—a diagnosis of blackwater fever is preferable to one of plasmoquine poisoning.

"On the other hand, when the guide-posts are methaemoglobinuria and cyanosis, plasmoquine toxicity suggests itself, to the exclusion of blackwater fever."

The remainder of this paper consists of clinical details of the 5 isolated cases of the series; and the last paper gives information regarding the 5 cases which occurred at the big headquarters station at Quetta, "where there are well qualified specialists and an excellent laboratory at the call of the ward medical officers."

With reference to the two diagnostic points mentioned above, Amy states that it is, of course, very desirable to determine spectroscopically which form of haemoglobinaemia was present. There is apparently no satisfactory evidence. In the description of Case 4 of the Quetta patients, we read :—

"Unfortunately, at Quetta there is no spectroscope.* Methaemoglobinaemia was presumed on the dark grey colour of the blood (it was impossible to match the specimens with the standard colours of the Tallquist haemoglobinometer); and methaemoglobinuria on the 'stout' as opposed to the port-wine colour of the urine. But for this, we have here a fairly complete and convincing picture, the outstanding features of which seem to be :—

"Sudden onset and dramatic swiftness of the attack.

"Rapid and massive destruction of the red blood cells.

"Methaemoglobinaemia, methaemoglobinuria and anuria.

"An attack out of all proportion to the amount of plasmoquine given; and a fatal issue despite the early withdrawal of the drug. Was the drug responsible?"

In the protocols of the Peshawar case we read :—"Urine, oxyhaemoglobin by the spectroscope +"; and in those of the first Kohat case "urine, spectroscopically, oxyhaemoglobin; presence of methaemoglobin doubtful," and 4 days later "spectroscopic bands of oxyhaemoglobin persist; with a suspicion of methaemoglobin." The only reference to the point at issue in the second Kohat case is that the urine "is markedly haemoglobininuric (port wine) in character."

With reference to the second diagnostic point, viz., cyanosis, the author states that although it may be difficult to detect in Indians when it is of mild degree, it is quite easy to recognize when severe as was the case in the Quetta patients.

[The reviewer has examined these papers with great care and has failed to discover any reason why the cases should be regarded as other than ordinary blackwater fever. The papers are lengthy and the introduction of numerous quotations and extracts from the writings of others makes it very difficult to follow the author's argument. Apparently the points against blackwater are :—(1) The patients are all Indian, (2) they had methaemoglobinaemia and methaemoglobinuria, and (3) they were cyanotic. As regards the first point much more must be known before we can attach any weight to the argument; no

*Similarly for Fort Sandeman and Wana. There are spectroscopes at Peshawar and Kohat.

evidence is produced that the patients did exhibit methaemoglobin to the exclusion of oxyhaemoglobin; and the third point does not seem to be very weighty. It is, of course, possible that plasmoquine was the factor which precipitated an attack of blackwater fever in these cases, but even this is doubtful because six of them had quinine as well as plasmoquine, three of them had atebirin, and one both quinine and atebirin].

W. Y.

HASSELMANN (C. M.). **Blackwater Fever in the Philippine Islands.**—*Jl. Philippine Islands Med. Assoc.* 1934. Jan. Vol. 14. No. 1. pp. 18-24. [12 refs.]

After drawing attention to the fact that the prevalence of blackwater fever is most unequal in different malarious countries, the author states that in the Philippine Archipelago and in most other parts of Malaysia the disease is rare and of a relatively mild nature.

He reports in detail a case of blackwater in a Japanese who resided for about 10 years in the Philippines and had never previously been sick.

The following summary is given.—

"1. Blackwater fever as a sequel to malaria is rare in the Philippine Islands.

"2. Only a single case, the report on which contains sufficient detailed data to establish the diagnosis beyond any doubt, had been reported previously.

"3. A second case of subtertian malaria with blackwater fever is presented, and its epidemiology, parasitology, clinical symptomatology, and therapy are briefly discussed.

"4. Several other cases are reported in the literature in which, however, the given data are not sufficient to establish their authenticity.

"5. The scanty loimological data on blackwater fever in the Philippines are cited and discussed."

W. Y.

JOFFÉ (Hillel). Contribution à la pathogénie et à la thérapeutique des fièvres hémoglobininuriques. [**Pathogenesis and Therapy of Blackwater Fever.**—*Jl. Egyptian Med. Assoc.* 1933. Oct. Vol. 16. No. 10. pp. 1022-1026.

This paper consists of a general discussion of the pathogenesis of blackwater fever and contains little that is new.

The author remarks that among the very numerous cases of blackwater fever which he has encountered during almost 40 years of work in Palestine he has met with 3 patients who had not taken quinine before the onset. The first was the case of a boy admitted in a comatose state with a high temperature, with pronounced jaundice, and with haemoglobinuria; he died almost immediately. The other two cases occurred in patients suffering from chronic malaria who had been given methylene blue. It is stated that in almost all the cases in which information was available regarding quinine, the attack of blackwater commenced about 5 hours after the administration of the drug.

The distribution of blackwater corresponds in general with that of pronounced malaria, but it is not always the case; thus, the disease is rare in the Roman Campagna, in certain notoriously malarial districts

of Greece, in Morocco, in Algiers, in Tunis, in Egypt, etc. It follows, therefore, that besides malaria and quinine, other factors play a part.

The author observed numerous cases which recovered after an intramuscular or intravenous injection of a large dose of quinine, and mentions the contradictory statements which the literature contains on this subject. Most authors state that cold is one of the provocative factors in blackwater fever, but the author's observations do not confirm this. He gives the monthly distribution of 202 cases seen by him in Palestine. The greatest number of cases occurred in September and October, which are not cold months. Attention is drawn to the fact that different epidemics may exhibit marked differences in intensity and in mortality. The author then passes into a discussion of the question of haemolysis in general and of that in blackwater fever in particular. He refers particularly to the experiments of WIDAL, ABRAMI, and BRISSAUD on autolysins, and to the work of NOCHT and KESSLER on the haemolytic action of the organs of blackwater patients. As a result of his reflections, the author reaches the conclusion that the same factor (cold or quinine) acting for a little time may increase haemolysis, but if its action is more prolonged or more intense it may diminish or stop haemolysis. For this reason he has for many years commended the use of colloidal quinine (Collobiase de quinine Dausse) in the treatment of blackwater fever. Each ampoule contains 0.0025 gm. of quinine, and the author injects the contents of 3 or 4 ampoules every 2 hours. He claims that his results are excellent.

W. Y.

WAYL (P.). **Observation of Blackwater Fever in Galilee.**—*Folia Medicinæ Internæ Orientalia*. Jerusalem. 1933. May. Vol. 1. No. 2. pp. 195-199.

The author has analysed the histories of 13 cases of blackwater fever in Galilee and has drawn therefrom certain conclusions.

Of the 13 cases 10 came from the Huleh area and 3 from the Jordan valley; 8 of the patients were born in Palestine, 3 immigrated when young, and 2 had been in the country for 4½ years, when they first developed blackwater.

The author summarizes his conclusions as follows:—

- " 1. Blackwater fever is still a frequent disease in the Huleh area.
- " 2. The morbidity and mortality is larger among Sephardic than among Ashkenazic Jews.
- " 3. The single attack of blackwater brings no immunity—just the reverse was observed.
- " 4. The disease seems to prevail in certain families; be it owing to physiological reasons or to certain habits (indifference towards treatment of malaria).
- " 5. No thermal repartition of blackwater fever was observed by us.
- " 6. At certain periods there is an increase of incidence, probably in connection with increase of malaria.
- " 7. In our experience quinine was the factor determining the onset of blackwater fever in the majority of our cases.
- " 8. A gradual administration of quinine to these patients does not prevent the blackwater fever.
- " 9. Quinine treatment is to be advised only in those cases of blackwater fever where malaria parasites are found.
- " 10. Blood transfusion, a new therapeutical procedure, seems to be quite safe, but is by no means a universal remedy."

W. Y.

NÄGELSBACH (Eduard). Schwarzwassergefieber und Atebrin. [**Blackwater Fever and Atebrin.**].—*Arch. f. Schiffs- u. Trop.-Hyg.* 1933. July. Vol. 37. No. 7. pp. 337-339.

An account is given of a case of malignant tertian malaria in which quinine provoked a slight attack of blackwater; atebrin cured the malaria infection and the haemoglobinuria quickly disappeared.

Atebrin has been shown to exert a powerfully parasitocidal action on the schizonts of *P. falciparum*, but whether it ever provokes an attack of blackwater is still an unanswered question.

The patient was a pregnant woman who arrived in hospital in the middle of the night. She had had a rigor during the morning and the blood contained numerous *P. falciparum*. She had not taken any quinine, as previously it had provoked an attack of blackwater. On admission labour had already commenced, but the pains were few and feeble. Atebrin 0.1 gm. was immediately given and a second tablet the next morning. The pains continued to be weak and it was decided to give an intravenous injection of solvochin (0.5 gm. of quinine HCl.). An hour later she passed black water. Some hours later thymophysin (10 units) was given, the pains increased and she was delivered of a healthy child. The urine cleared soon after parturition. On the same day, 5 hours after the appearance of blackwater, another tablet of atebrin was given, and 2½ tablets (0.25 gm.) on each of the 4 following days. There was no further fever and no more haemoglobinuria.

W. Y.

MOIR (K. Tole). **Blackwater Fever following Atebrin.**—*West African Med. J.* 1934. Jan. Vol. 7. No. 3. pp. 121-123.

Records are given of two cases of blackwater fever following the administration of atebrin. The author considers the matter is of importance and should be generally known, the more especially because the manufacturers state that atebrin is "not contra-indicated in blackwater fever."

Case 1. Veterinary officer, aged 31, took ill with fever on the 23.9.33. On Sept. 26th *P. falciparum* infection was diagnosed and a course of atebrin and plasmoquin simplex (3 tablets a day for 3 days) recommended. The patient had been in the habit of taking prophylactic quinine, 5 gr. daily, but discontinued this whilst taking atebrin. He suffered from marked abdominal symptoms and vomited. The next day he still felt bilious, so did not take the last of the atebrin plasmoquin tablets. On Oct. 3rd he felt well all day and played polo in the evening. Later, however, his temperature rose to 100°F. On Oct. 4th, as he was still feverish, he took 5 gr. of quinine about 8 a.m.; at 9.15 p.m. he had a rigor and passed black water later in the evening. The attack was a mild one.

Case 2. Veterinary officer, aged 26. This officer was sent to relieve the previous one when he fell ill. He also was in the habit of taking the daily prophylactic dose of quinine. He contracted subtertian malaria and was given the same course of atebrin and plasmoquin simplex as was the previous case, but, on the recommendation of his doctor, he continued his daily dose of 5 gr. whilst taking the atebrin. He completed the course of treatment on Nov. 3rd. The next morning he took his customary 5 gr. of quinine and felt well during the day, but in the evening had some malaise. He went to bed early and had a severe rigor about 10 p.m. and took 10 gr. quinine and 10 gr. of aspirin. About midnight he passed black water; this attack was also mild.

Discussing these cases, the author writes that it is obvious that the course of atebrin plasmoquine failed in two respects, viz. :—

- " 1. It did not prevent the onset of blackwater fever.

" 2. If one agrees with the hypothesis that blackwater fever is always a complication of malaria then a full course of atebirin with plasmoquin cannot have got rid of the malarial infection in these cases. This is borne out by the presence of parasites in the blood of Case 2.

" The questions suggested by these cases are as follows :—

" 1. Are they examples of failure of the specific action of atebirin, the drug being in good condition, or was the failure due to some other cause ?

" 2. Were the attacks of blackwater fever directly excited by the atebirin-plasmoquin taken ? "

It is difficult to answer the first question. There seems to be no evidence that the drug had undergone any deterioration, or that the patients had failed to take the course of treatment conscientiously and regularly. As regards the question whether the blackwater fever was directly excited by the atebirin-plasmoquine course, the author states that this can best be answered by considering first what other exciting cause there may have been. It might be argued that the resumption of the daily prophylactic quinine in Case 1 was the exciting factor, but such a conclusion is completely negatived by Case 2, in which the daily quinine was taken throughout the atebirin course. After considering all the circumstances, Moir writes " The fundamental conclusion remains that under certain circumstances, which cannot be defined, atebirin and plasmoquine is not only incapable of preventing blackwater fever, but will probably excite an attack." This conclusion, in Moir's opinion, is of the greatest importance and discredits the claim that atebirin is not contra-indicated in blackwater fever. He does not mean that atebirin is not a valuable drug in the treatment of malaria, but that it cannot be regarded as safe, and must be placed in the same category as quinine, and " given with the same degree of caution in subtertian malaria when a possibility of blackwater fever exists." [It would considerably assist the reviewer and doubtless many others if the author would let us know what exactly this last sentence means.]

W. Y.

PATERSON (James C.). **Note on the Use of Alkali Therapy in the Treatment of Blackwater Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1933. May. 5. Vol. 26. No. 6. pp. 539-546.

Observations are recorded on a number of cases of blackwater fever from the interior of Colombia, some of which were treated by early injections of sodium bicarbonate. These observations were made because of the considerable difference of opinion regarding the value of the intravenous injection of sodium bicarbonate during the acute stage of blackwater fever expressed at a recent meeting of the Royal Society of Tropical Medicine and Hygiene [this *Bulletin*, Vol. 30, p. 518].

Each of the patients received treatment with sodium bicarbonate, but the method of administration varied in different cases. The patients were divided into three main groups.

Group I received sodium bicarbonate by the mouth only. It consisted of 13 cases at the El Centro Hospital. In five of these the urine was alkaline before treatment was commenced, and it continued in this state throughout the duration of the haemoglobinuria; one of these died, but there is some doubt whether the case was really blackwater and not plasmoquine poisoning. The other 8 cases exhibited strongly acid urine at the onset of blackwater; in two of these the reaction became alkaline during treatment and both recovered; in the remaining

six the urine continued to be acid, notwithstanding the alkaline treatment, and four of them died.

Nine cases were also treated in this way in other of the Company's hospitals. Although the records are by no means complete, apparently the urine in each patient was acid or neutral at the onset of blackwater. In two the urine became alkaline during treatment and both recovered; of the remaining seven, three died, and in at least two of the fatal cases the urine retained its acid character throughout the duration of haemoglobinuria.

Group II received, in addition, an intravenous injection of sodium bicarbonate at a late stage of the disease when a urinary suppression was threatened. Two cases were treated in this way at the El Centro Hospital, and in both the urine became alkaline almost immediately after the injection was given; one of the patients who had definite suppression of urine at the time of the injection died 18 hours later, the other recovered.

Of the three patients treated in this way at other hospitals, one died.

Group III were given an intravenous injection as soon as the diagnosis was made, and following this sodium bicarbonate was continued by the mouth. In each of the 5 cases treated in this way at the El Centro Hospital, the urine was strongly acid before the injection, but in every case subsequent specimens of urine were alkaline; all the patients recovered.

Of the 4 cases treated at other hospitals by this method two died.

Details of all these cases are given in tables from which it is seen that the mortality among the 36 cases was 12 (33 per cent.). Of the 22 cases in Group I, eight (36 per cent.) died; in five of these the cause of death was suppression of urine, in one suppression and shock following a miscarriage, in one suppression and plasmoquine poisoning (?), and in one subtertian malaria and partial suppression of urine. Of the five cases in Group II, two (40 per cent.) died, both from suppression of urine. Of the 9 cases in Group III, two (22 per cent.) died, both from acute anaemia, cyclical vomiting, and possibly alkalosis.

The following are the author's conclusions:—

"1. The prognosis in blackwater fever appears to be relatively good in cases which show an alkaline reaction of the urine at the onset of haemoglobinuria. In the eighteen cases of our combined series in which this reaction was either naturally present or was artificially produced by alkalization at an early stage of the disease, the mortality was less than 17 per cent., and in only one of the three fatal cases was urinary suppression present.

"2. The oral administration of sodium bicarbonate was found to be insufficient to render the urine alkaline in 75 per cent. of the cases which received it in this manner only. On the other hand, the urine was almost immediately alkalized following the injection of sodium bicarbonate solution intravenously.

"3. The practice of injecting sodium bicarbonate solutions intravenously after signs of urinary suppression have developed is worth a trial, but is probably of little value. Of the five cases which received it in this manner 40 per cent. died.

"4. The early administration of intravenous sodium bicarbonate solution in our series of nine cases appears to have had a preventive action on the development of urinary suppression. As this is the principal cause of death in blackwater fever, I believe that such a procedure is justified in all cases which are seen in their early stages. Providing that certain precautions are taken, the danger of producing an unfavourable reaction appears to be slight; the injection should not be given (nor should it be

repeated) in the presence of an alkaline urine, and the solution should be sterilized before, and not after, the addition of the bicarbonate."

W. Y.

ALAIN (M.). A propos de deux cas de fièvre bilieuse hémoglobinurique et de leur traitement par la quinacrine. [**The Treatment of Two Cases of Blackwater Fever by Quinacrine.**]—*Bull. Soc. Path. Exot.* 1934. Jan. 10. Vol. 27. No. 1. pp. 93-97.

BLONDIN (P.) & RIOU (M.). Quinacrine et fièvre bilieuse hémoglobinurique.—*Ibid.* pp. 97-98.

Each of these papers gives details of 2 cases of blackwater fever which were treated with quinacrine; all the patients recovered.

The dose of the drug was 2 or 3 tablets, each containing 0.1 gm. of quinacrine, daily. It is claimed that there was an immediate improvement in symptoms, that the blood was quickly sterilized, and that there were no untoward effects.

BLANCHARD, in the discussion which followed the reading of these papers, pointed out that, apart from its quite special indication in blackwater fever, it must be remembered that quinacrine has a remarkable action on the schizonts of *P. falciparum*, and on both the schizonts and gametes of *P. vivax* and *P. malariae*.

W. Y.

FAIRLEY (N. Hamilton) & BROMFIELD (R. J.). **The Determination of Haemoglobinaemia and Methaemoglobinaemia in Blackwater Fever.** [Laboratory Meeting Demonstration.]—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Jan. 31. Vol. 27. No. 4. pp. 335-336.

— & —. **Laboratory Studies in Malaria and Blackwater Fever. Part II. Blackwater Fever. Haemoglobinaemia.**—*Ibid.* Aug. 4. Vol. 28. No. 2. pp. 141-156. With 2 graphs & 1 coloured plate. [15 refs.]

In these papers the authors concern themselves with the very important subject of haemoglobinaemia in blackwater fever. A method is described for the quantitative determination of oxy- and met-haemoglobinaemia, and the results obtained in a series of blackwater fever cases are given. Some information is also provided regarding a new blood pigment.

The second paper opens with a brief summary of the earlier reports on haemoglobinaemia in blackwater fever. As the summary shows, practically no quantitative observations had been made, apart from those of the reviewer and his colleagues. Methaemoglobinaemia has occasionally been noted, but its presence has evoked surprisingly little comment. ARKWRIGHT and LEPPER (1918) recorded its presence in the serum and plasma of one or two cases, and YORKE, MURGATROYD and OWEN (1930) noted the presence of methaemoglobinaemia in the plasma, but not in the corpuscles of two cases—in the first on the 3rd, 4th and 5th days of the disease and in the second on the 4th day only. ROSS found methaemoglobinaemia in 12 of his 18 cases in which special attention was directed to the spectroscopic appearance of the plasma.

The technique used in the quantitative estimation of haemoglobinaemia is as follows:—

Method of collecting blood.—The first essential is to collect blood by a technique which produces a minimum damage to the red cells and so avoids artificial plasmolysis. It was found that "true plasma" obtained from blood aspirated from the median basilic vein under paraffin, and

subsequently oxalated and centrifuged under paraffin, afforded the best technique for this purpose. "True plasma" showed no trace of haemoglobin bands in 46 of 53 control cases, whilst in the remaining 7 cases the haemoglobin varied from 0.07 to 0.12 per cent. From this it is concluded that plasma haemoglobin must exceed 0.12 per cent. before it can be regarded as significant of haemoglobinaemia.

Spectroscopic method for quantitative estimation.—The technique employed is that of Bloem.* It is briefly as follows:—

The minimum concentration at which the α band just disappears from standard solutions of haemoglobin and methaemoglobin equals 0.33 per cent. and 0.665 per cent. respectively; using the same standard cell, the degree to which the unknown plasma has to be diluted to obliterate the band is similarly determined; the concentration of pigment in the unknown is then ascertained by multiplying this standard value by the dilution factor.

Nine cases of blackwater fever were investigated, and in five of them serial quantitative observations were carried out. The case history and other relevant data of each case are given. The quantitative determination of the oxyhaemoglobin and methaemoglobin made in four of the cases is summarized in the following table:—

Cases.	Time after onset in hours.	Percentage.		
		Oxyhaemoglobin.	Methaemoglobin.	Total of haemoglobin.
3	4	1.4	1.3	2.7
	21½†	1.35	2.26	3.6
	46	1.0	2.3	3.3
4	4½	0.83	1.33	2.16
	16½†	0.20	1.66	1.86
	23	0.36	1.0	1.36
	40½	0.13	1.0	1.13
	63½	0.13	0.66	0.79
5	22	0.26	1.33	1.59
	47½	0.07	1.33	1.4
6	15	2.48	2.66	5.14
	19	2.15	2.66	4.81
	24	1.75	2.66	4.41
	35	1.16	3.33	4.49
	39½	0.76	3.33	4.09

†Blood transfusion was performed immediately after this specimen was collected.

In all their estimations true plasma was used, and the authors claim that as the risk of artificial plasmolysis was thereby reduced to a minimum, the discoloration of the plasma observed in several of the cases finally disposed of any argument as to whether the haemoglobinaemia may or may not be intense enough to be recognized by the naked eye. One specimen is depicted in a coloured plate. Several different constituents enter into the final discoloration of the plasma. Oxyhaemoglobin produced a rose-red, methaemoglobin a brown, and

*Bloem, 1933. *Biochemical Jl.* 27, 121.

bilirubin a yellow appearance, and the extent to which one or other of these pigments predominates determines its final appearance. Deep red and brownish red plasma all appear to contain methaemoglobin.

Methaemoglobin was observed in every instance except Case 8, where an entirely new pigment was encountered. In this case a peculiar feature of the illness was the leaden-grey colour of the skin and the mauve tinting of the lips and ears. The plasma until the 11th day contained a brownish pigment resembling methaemoglobin spectroscopically, but unlike it in not being reduced by Stokes' reagent or by ammonium sulphide. This pigment was never found in the urine, although methaemoglobin was demonstrated in numerous urinary specimens. Investigation by KELLIN indicated that it was a new blood pigment—probably some modification of methaemoglobin—details of which will be published later.

The red corpuscles from these cases, after being washed with saline and subsequently lysed in distilled water, exhibited no trace of methaemoglobin; the rapidity with which these blackish corpuscles regained their normal reddish colour during washing was very striking.

Quantitative estimations in both fatal and non-fatal cases revealed the unexpected fact that methaemoglobin constituted the major portion of the total blood pigment in the haemoglobinaemia. In the fatal cases the oxyhaemoglobinaemia decreased progressively as the methaemoglobinaemia increased. This suggests either an accumulation of methaemoglobin due to the body being unable to destroy or excrete it at the same rate as oxyhaemoglobin, or, alternatively, that as the disease progressed more and more plasma methaemoglobin was produced from oxyhaemoglobin.

In the fatal cases the maximum amount of blood pigment in the plasma (oxyhaemoglobin + methaemoglobin) amounted to 3.6, 4.61, and 5.14 per cent. respectively. Possibly, more numerous observations would have resulted in even higher maximal readings. It appears, therefore, that the haemoglobinaemia in blackwater fever is not nearly as small as was previously thought, and is in fact sufficient to explain the phenomena in blackwater fever in terms of an intravascular haemolysis, without postulating that haemolysis is proceeding in the byways of the spleen and other internal organs shut off from the peripheral circulation. In blackwater fever the methaemoglobin appears to arise from oxyhaemoglobin, which has been liberated from the corpuscles after lysis. In this respect, the methaemoglobinaemia encountered in blackwater fever differs fundamentally from that induced by certain drugs where the methaemoglobin so often has an intra-corpuscular location, and in the absence of haemolysis may fail to appear in the plasma or to be excreted in the urine.

W. Y.

MINATOYA (Takeo). Durch Hämoglobininjektion verursachte Hämoglobinurie. [**Haemoglobinuria due to Haemoglobin Injection.**]—*Tohoku Jl. Experim. Med.* 1934. Sept. 28. Vol. 24. Nos. 1 & 2. pp. 11–20. [11 refs.]

The experiments described in this paper were undertaken mainly with the object of ascertaining whether the haemoglobin which appears in the urine of an animal which has received an intravenous injection of heterologous or isologous haemoglobin, is derived entirely from the injected haemoglobin or in part from the animal's own erythrocytes.

Immune sera were prepared firstly by injecting rabbits with horse haemoglobin, and secondly by injecting guineapigs with rabbit haemoglobin. A number of rabbits were then given an injection of horse haemoglobin and the resulting haemoglobinuria examined by the precipitin test with the above sera. The result indicated that the haemoglobin in the urine was derived entirely from the horse haemoglobin.

Examinations were then made of the number and volume of the erythrocytes in rabbits at various intervals after intravenous injection of horse or rabbit haemoglobin. It was found that there was a fall both in the number and volume of the red cells, and that this was greater after the injection of horse haemoglobin than after rabbit haemoglobin. In later experiments so much haemoglobin was given that the animals were reduced to a critical condition; although a fall in the erythrocyte number and volume was observed no evidence of the host's haemoglobin could be found in the urine. [There seems to be a possible fallacy in the author's assumption that the cause of the fall in the erythrocyte number and volume seen in the experimental rabbits was due to a destruction of erythrocytes consequent upon the haemoglobin injection. It is, of course, impossible to form any definite opinion on the matter unless we know that the blood volume did not alter. If there was any increase in blood volume after the injection there would naturally be a fall in the apparent erythrocyte number and volume, even though the erythrocytes themselves were completely uninfluenced by the haemoglobin injection.] W. Y.

VOIGT (E. M.) & VOIGT (C.). Ueber antihämolytisches Serum (Versuche zur Schwarzwasserfieberfrage). (Vorläufige Mitteilung.) [**Antihæmolytic Serum. Experiments on the Blackwater Fever Problem.**—*Arch. f. Schiffs- u. Trop.- Hyg.* 1934. June. Vol. 38. No. 6. pp. 232-243. [21 refs.] English summary.

The work here described was undertaken with the object of studying the hæmolytic process in blackwater fever, and with the hope of discovering some substance which will counteract the hæmolysis.

As the authors rightly observe, in order to prevent the action of a hæmolysin it is necessary to discover something about that hæmolysin and to prepare a specific antihaemolysin. It is possible that the destruction or damage of the red cells in blackwater is dependent upon the failure of certain substances in the serum or in the blood cells which are necessary for their integrity and for their protection against the influence of external bodies. With this idea in mind the authors have commenced an investigation of several aspects of the blood chemistry in blackwater fever; lipid metabolism in particular seemed to be a promising field for investigation.

There is a general notion that a lowering of the cholesterin content of the serum or red corpuscles is related to a tendency to the disintegration of the latter. The authors employed Bloor's method which consists in making an alcohol-ether extract of blood—cells and serum—as for the estimation of the total fats. Up to the present they have failed to observe any specially low values; in whole blood and in red cells the values obtained were somewhat higher than for the serum. After recalling that in acute nephritis hypercholesteræmia is the rule, whilst in chronic interstitial nephritis, with retention of nitrogen but without oedema, an increase of the cholesterin value is

found, the authors state that it seems to them to be important to determine whether in recurrent blackwater cases the red cells habitually contain more cholesterol than normally.

MATKO put forward the theory that phosphate metabolism played a part in the haemolysis of blackwater fever [this *Bulletin*, Vol. 12, p. 358] and the question has been recently examined by WHITMORE, who also observed the interesting fact that in two cases of blackwater the lecithin content of the blood was considerably below normal [*loc cit.*, Vol. 26, p. 1026].

The authors themselves have not yet had the opportunity of determining the lecithin content of the washed red corpuscles from cases of blackwater fever, but the point must be investigated. According to MEYER and OVERTON (1901) the stroma of the red cell consists one-third of lipoids and two-thirds of protein; any factor which decreases the phosphorus content of the red cell interferes with the functioning of the cell membrane and may lead to disintegration of the cell. The organic phosphate content of the serum has been determined in various cases, but so far it has never been found to be definitely lowered.

Impressed by recent work upon disappearance of serum complement in acute conditions, the authors have attempted to produce evidence of unexpended haemolysin in the sera of blackwater fever cases by the addition of fresh guineapig serum. While freely admitting that there is no definite evidence that any serum haemolysin is at work in any stage of blackwater fever, it nevertheless seemed reasonable to the authors to seek a substance capable of neutralizing antihuman haemolytic amboceptor, and to try it as a remedy and to examine its effect, if any, upon the known death rate and relapse incidence. They claim to have produced, by injecting haemolytic sera into baboons, pigs, and a few human volunteers, sera which inhibit the action of anti-human haemolytic amboceptor. The antibody produced in the human beings is upon trial in blackwater fever cases in Rhodesia and South Africa.

W. Y.

GIGLIOLI (George). **Further Studies on the Epidemiology and Etiology of Blackwater Fever in the Interior of British Guiana. Immunity in Blackwater Fever.**—*Riv. di Malariologia*. 1932. Nov.-Dec. Vol. 11. No. 6. pp. 785-807. With 4 figs. [15 refs.]

This paper, which reports on certain epidemiological characteristics of blackwater fever on the Demerara, tending to throw light on the very difficult problem of immunity in blackwater fever, was published elsewhere and was noticed in this *Bulletin*, Vol. 30, p. 517. W. Y.

THÉMELIN. Un cas de transfusion avec résultat favorable chez un malade atteint de fièvre bilieuse hémoglobinurique grave. [**A Case of Blackwater Fever Successfully treated by Transfusion.**—*Bull. Méd. du Katanga*. 1933. Vol. 10. No. 4. pp. 95, 97-98.]

Details are given of a severe case of blackwater fever, which recovered after blood transfusion. W. Y.

PERATONER (U.). L'emoglobinuria nella malaria. (Contributo clinico e terapeutico).—*Riv. di Malariologia*. 1934. Vol. 13. No. 1. pp. 58-65. [16 refs.] French summary (5 lines).

MISCELLANEOUS.

STRAUSS (Maurice B.). **The Rôle of the Gastro-Intestinal Tract in conditioning Deficiency Disease. The Significance of Digestion and Absorption in Pernicious Anaemia, Pellagra and "Alcoholic" and Other Forms of Polyneuritis.**—*Jl. Amer. Med. Assoc.* 1934. July 7. Vol. 103. No. 1. pp. 1-4. [48 refs.] [Summary appears also in *Bulletin of Hygiene.*]

Deficiency disease in man may and frequently does develop owing to some disturbance in the gastro-intestinal tract in spite of an adequate diet. Pernicious anaemia is a deficiency disease due to the absence from the gastric juice of a specific heat-labile factor which reacts with an extrinsic factor contained in the food. It may result in the presence of an adequate diet and normal gastric juice where there is inadequate absorption from the intestine. It has been observed in chronic bacillary dysentery and in coeliac disease and in strictures and multiple anastomoses in the intestine. Surgical relief of the stricture has resulted in cure of the anaemia. The author observed a case of pernicious anaemia in a boy of 8 years due to short-circuiting between intestinal loops. At least 4 of this type of case have been relieved of their anaemia by liver therapy alone without operative treatment. Pellagra, in the endemic form, is probably due to lack of vitamin B₂ in the diet, but in the North (U.S.A.) it is seen, with rare exceptions, in persons with lesions or abnormalities of the gastro-intestinal tract or in chronic alcoholic addicts. In alcoholics a moderately faulty diet may also play a part. All types of gastro-intestinal lesions have resulted in pellagra; amongst the commonest are cancer of the stomach (usually with pyloric obstruction), rectal stricture, ulcerative colitis, gastro-enterostomy and the author has seen it in mucous colitis, duodenal ulcer, diaphragmatic hernia and stenosis of the small intestine. In most of the author's cases the lesion has prevented the taking of an adequate diet, but in at least ten cases the diet was entirely adequate. Polyneuritis is rarely seen in the North except when it is conditioned by gastro-intestinal factors, the most common of which is chronic alcoholism. It was previously shown that over 80 per cent of cases of alcoholic polyneuritis had gastric anacidity or hypoacidity and that 95 per cent. had partaken of grossly inadequate diets. Recently 6 patients of this type were given 1-2 pints of whisky (or the amount usually taken) daily, and relief of the neuritis was obtained by oral or hypodermic administration of large quantities of vitamin B. The "toxic" polyneuritis of pregnancy occurs only after "pernicious vomiting"; the author has recorded 3 cases cured by giving adequate amounts of vitamin B. Polyneuritis has been reported as following persistent vomiting due to several causes and associated with various gastro-intestinal lesions. Beriberi has also been observed to follow gastro-intestinal trouble (*e.g.*, coeliac disease, chronic dysentery, etc.). Hypochromic anaemia is another example of faulty absorption (due to achlorhydria), and the "toxic" state of intestinal obstruction is probably a manifestation of a deficiency of water and electrolytes rather than of a toxæmia.

H. N. H. Green.

DOBREFF (Minko). Ueber die Selbstvergiftungen mit Chinin in Bulgarien. [**Self-Poisoning with Quinine in Bulgaria.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. July. Vol. 38. No. 7. pp. 288-291.]

In the last four years in one-third of the cases of poison self-administered in Bulgaria quinine was the agent used, and at the University Clinic at Sofia in the last 7 years 82 quinine cases have been admitted against 51 self-poisonings with other substances. The chief cause seems to be the popularity of this drug for "stimulating menstruation," and this is supported by the observation that of 86 patients 69 were women, and nearly all under 30. The average quantity of "quinine" taken was 4-6 gm.; the largest dose 16 gm. All recovered. Some had albuminuria with red cells in the urine, others amblyopia or temporary loss of vision. [Nothing is said of deafness or other symptom, nor do we learn what proportion of the women were pregnant. In his conclusions the author writes of "Chininselbstmordversuche," but it seems doubtful whether all these attempts were suicidal.]

A. G. B.

GHOSE (A. K.). **Naga Sore in a Tea-Estate Practice.**—*Indian Med. Gaz.* 1934. June. Vol. 69. No. 6. pp. 316-318.

The author's account of Naga sore or tropical phagedaenic ulcer agrees with other accounts in that it occurs in coolies doing outdoor work, is usually preceded by a prick or injury of some kind, and is mainly found on the legs below the knees. Like others he suggests soil infection. It appears at the beginning of the rains, attaining its maximum in June and July, the busiest season of the year, and disappearing in December. The average period of disability was 38 days. He states that 20 per cent. of newly recruited coolies were affected and only about 2 per cent. of old coolies [but the numbers are small]. He cauterizes thoroughly with pure carbolic acid and after separation of sloughs dresses antiseptically. He advocates for prevention compulsory leg washing in an antiseptic solution.

[A useful editorial appears in the same number. The possible association with soil is mentioned, but not the suggestion of J. A. YOUNG that "the reservoir of infection may lie in the termite's nest" (this *Bulletin*, Vol. 29, p. 525). Perhaps in India this affection occurs where termites are absent.]

A. G. B.

NADLER (J. Ernest), GREEN (Henry) & ROSENBAUM (Arthur). **Intravenous Injection of Methylene Blue in Man with Reference to its Toxic Symptoms and Effect on the Electrocardiogram.**—*Amer. Jl. Med. Sci.* 1934. July. Vol. 188. No. 1. pp. 15-21. With 1 fig. [22 refs.]

Methylene blue has been used in various conditions, including malaria and leprosy. The authors gave 18 normal adults 50 cc. of a 1 per cent. solution; elimination of the dye took 3 to 5 days; two persons received three injections. The drug was found to have two actions: it oxidized some of the haemoglobin to methaemoglobin and produced restlessness, paresthesia, "burning" in mouth and stomach, pain in chest and strangury, the manifestations lasting 24 to 48 hours. It had also an effect on the electrocardiogram. The authors "wish to point out that the indiscriminate use of methylene blue may produce unpleasant results and be dangerous to the patient."

A. G. B.

FIGULEWSKY (S. W.). Einige klinische Beobachtungen ueber die Wirkung des Skorpiongiftes auf den Menschen. [*Clinical Notes on the Action of Scorpion Poison on Man.*].—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Aug. Vol. 38. No. 8. pp. 350–355. With 2 figs. [33 refs.]

The author's observations were made in the Karakal steppe region in Russian Turkestan and he describes the symptoms with much detail in three cases. Twelve species of scorpions have been described from the U.S.S.R. In the Karakal steppes they appear in May and early in September near houses and stables; they sting in May, rarely in the autumn. The symptoms last as a rule from 2 to 5 days. A fatal result is rare. A. G. B.

DO AMARAL (Afranio), APANTES (J. Bernadino) & DA FONSECA (Flavio). Sobre a duração da actividade das antitoxinas e antivenenos. [*Duration of Activity of Antitoxins and Antivenins.*].—*Brasil-Medico.* 1934. July 7. Vol. 48. No. 27. pp. 525–532. [22 refs.] English summary.

The English summary runs thus:—

"In the retitration of many samples of antitoxins and antivenines that had aged for a period sometimes as long as 25 years under ordinary conditions, without special preservation precautions, in the consumers' hands, many interesting facts have been disclosed. These may be briefly summarized as follows:—

"1. The precipitate formed with the ageing of antitoxins and antivenines and represented by pseudoglobulin seems not to exert any marked influence upon their activity.

"2. Neither the method of refination or concentration by fractionated precipitation of globulins as employed at the Instituto Butantan in its routine work since 1917, nor their final hydrogen ion concentration (pH) seems to contribute towards their inactivation even after a long ageing as proved by the retesting of samples of batches concentrated as nearly [? early] as 1916 at the Instituto Butantan.

"3. Ageing itself probably is not the cause of their (distribution) becoming more or less stabilized afterwards. Their inactivation at first may reach 50 per cent. of their primitive titer of which the loss seldom represents 66 per cent. (exceptionally 70 per cent.) even after 25 years of ageing.

"4. Therefore, there is no definite reason for aged antitoxins and antivenins to be entirely discarded from consumption inasmuch as virtually all producing laboratories leave a margin of safety in the titer borne on the label of the ampoules of each batch they prepare."

HOVERSON (Emil T.) & PETERSEN (William F.). **Meteorologic Effects on the Sedimentation Rate of Erythrocytes.**—*Amer. Jl. Med. Sci.* 1934. Oct. Vol. 188. No. 4. pp. 455–461. With 1 chart.

An interesting article and a timely warning to those who are inclined to rush to conclusions based on their findings of the rate of sedimentation of red corpuscles in disease and in health. Stress has been laid on the sedimentation rate in malaria, in leprosy, in tuberculosis and other conditions (see NEWHAM, this *Bulletin*, Vol. 25, p. 496).

It is fairly widely agreed that in acute infections the rate is hastened, and that as improvement occurs the rate falls. Others have found that there are daily variations in normal subjects; and it is certainly true that the rate differs in a tuberculous subject according to the presence or absence of fever.

The authors found that the method used, Linzenmeier's, or Westergreen's and Cutler's, did not affect the results. One of the authors has been investigating during the past six years the detailed physiological and pathological changes associated with meteorological alterations, and finds that "pressor episodes, falling carbon-dioxid and increasing blood pH, localized or general anoxemia, alternate with periods when the diastolic blood pressure falls, the carbon-dioxid content increases, the blood pH decreases, basal metabolism and oxidation increases." Daily determinations were made whenever possible on 12 subjects between 28th January and 1st March, 1934, and the results were graphed. This time of year was chosen because it is commonly a time when meteorological changes and disturbances are common in Illinois, and as a matter of fact there were 9 distinct disturbances in the period of observation.

The authors found that there are wide daily variations in rate of sedimentation of erythrocytes, amounting to as much as 100 per cent., and that there is a correlation between these daily variations and the meteorologic changes.

H. H. S.

LEAO (A. E. de Arêa). Sur une mycose osseuse par *Acremoniella*. Nouvelle espèce de champignon trouvée chez l'homme: *Acremoniella rugulosa* n. sp. [Mycosis of Bone due to *Acremoniella rugulosa* n. sp.]—C. R. Soc. Biol. 1934. Vol. 116. No. 26. pp. 1158-1160.

Infection of man by this genus has been observed only in Italy and now in Brazil.

A Brazilian resident of Rio de Janeiro, which he had never left, wounded his leg a year before with a splinter of wood; to which succeeded pain, swelling, abscess and fistulae. When seen there was oedema of the leg and at the upper third of the fibula three fistulas giving vent to yellowish pus. Above were gummas. A radiogram showed that the upper third of the fibula was affected and the head destroyed. No general reaction. Search for tubercle by Mantoux's reaction and inoculation of guinea pig was negative. A gumma was punctured, fluid was sown on glucose agar, and after 12 days the fungus developed. Its characters under the microscope and in culture are described. The case was treated surgically with success.

A. G. B.

MOORE (M.). *Posadasia pyriformis* and *P. capsulata*, Two Causative Organisms of Darling's Histoplasmosis in the United States.—*Ann. Missouri Bot. Gard.* 1934. Vol. 21. No. 2. pp. 347-348. [Summarized in *Rev. Applied Mycology*. 1934. Oct. Vol. 13. Pt. 10. p. 637.]

"Diagnoses are given in English and Latin of two fungal organisms, *Posadasia pyriformis* n. sp., and *P. capsulata* (Darling) Moore, n. comb. (syn. *Histoplasma capsulatum* Darling) associated with the human disease known as Darling's histoplasmosis, characterized by an acute specific infection usually affecting the epithelial and endothelial cells of the lungs, liver, and spleen. The organisms may also be present in a free state in these organs, as well as in the blood stream, reproduction in the host being by single yeast-like cells. In culture a

mycelium, conidia, chlamydospores, and multisporous asci are formed. Complete morphological, cultural, biochemical, and cytological details will be given in a subsequent paper."

- i. DE MONBREUN (W. A.). **The Cultivation and Cultural Characteristics of Darling's *Histoplasma capsulatum*.**—*Amer. Jl. Trop. Med.* 1934. Mar. Vol. 14. No. 2. pp. 93-125. With 1 fig. & 5 plates. [26 refs.]
- ii. DODD (Katharine) & TOMPKINS (Edna H.). **A Case of Histoplasmosis of Darling in an Infant.**—*Ibid.* pp. 127-137. With 13 figs. on 2 plates.

i. The paper describes the cultivation of *Histoplasma capsulatum*. The fungus may be grown either as a yeast or as a mycelium, the former being the actual pathogenic phase. Certain cultural characters suggest that the organism belongs to the Endomycetales group of fungi. The author proposes altering the well-known name of the disease caused by the fungus from Histoplasmosis of Darling to Cytomycosis of Darling, a procedure which hardly seems necessary.

ii. The authors describe a case of histoplasmosis in an infant six months old, a native of Tennessee. The diagnosis was made during life by the discovery of the characteristic yeast-like parasite in large mononuclear cells in the peripheral blood. It seems that these large mononuclear cells blocking the blood vessels and actively phagocytosing red blood corpuscles are responsible for most of the symptoms of the disease.

C. M. Wenyon.

REDAELLI (P.) & CIFERRI (R.). *Études sur l' "Histoplasma capsulatum" Darling*: I. Reproduction expérimentale de l'histoplasmosse, et définition de la maladie comme réticulo-histocytose parasitaire atteignant divers systèmes de l'organisme. [**Experimental Studies on *H. capsulatum*.**]—*Bol. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1934. June. Vol. 6. No. 6. pp. 193-195.

The author refers to the work of DE MONBREUN, who has cultivated *Histoplasma capsulatum* in two forms, as a yeast and as a mould. With the yeast form he states that he has been able to reproduce the human disease in monkeys only. The mould form he claims is not pathogenic to any animal. The present writer states that by inoculating the mould subcutaneously in guinea-pigs a local lesion is produced from which he obtained material which gave rise to the typical Histoplasma infection of the reticulo-endothelial system when inoculated into guinea-pigs and rabbits.

C. M. W.

CIFERRI (R.) & REDAELLI (P.). *Histoplasma capsulatum* Darling, the Agent of "Histoplasmosis": Systematic Position and Characteristics.—*Jl. Trop. Med. & Hyg.* 1934. Sept. 15. Vol. 37. No. 18. pp. 278-280. [13 refs.]

Having studied cultures of *Histoplasma capsulatum* the authors arrive at the conclusion that it belongs to the Blastosporales "sensu lato," of which it forms the type of a new family for which they propose the name Histoplasmaeae.

C. M. W.

SVENSSON (Ruth) with the co-operation of F. J. LINDERS. **The Chances of detecting Infections with Intestinal Protozoa. A Parasitological and Statistical Survey.**—*Acta Med. Scandinavica*. 1934. Vol. 81. No. 3/4. pp. 267–324. With 4 diagrams. [13 refs.]

As a result of an exhaustive examination of 74 persons in a mental hospital in Sweden, the author has found all the usual intestinal protozoa. By somewhat elaborate statistical calculations it is concluded that neither 3 examinations, nor even 6, of any two groups of individuals give sufficient indication of the actual infections present for the two groups to be compared. If, however, 10 examinations are carried out on the individuals of each group the results will be sufficiently accurate for purposes of comparison. C. M. W.

ANDREWS (Justin). **The Diagnosis of Intestinal Protozoa from Purged and Normally-Passed Stools.**—*Jl. Parasitology*. 1934. June. Vol. 20. No. 4. pp. 253–254.

Data are given showing that the single examination of a stool obtained after the use of a saline cathartic will reveal at least 75 per cent. of the protozoan infections which will be found by six or more examinations of normal stools. C. M. W.

HEGNER (Robert). **Intestinal Protozoa of Chimpanzees.**—*Amer. Jl. Hyg.* 1934. Mar. Vol. 19. No. 2. pp. 480–501. [35 refs.]

Examination of a number of chimpanzees has revealed intestinal protozoa which correspond so closely with those that occur in man that they cannot be distinguished from them morphologically. These are *Entamoeba* (of the *E. coli*, *E. gingivalis* and *E. histolytica* types), *Endolimax*, *Iodamoeba*, *Giardia*, *Chilomastix*, *Trichomonas* (intestinal and vaginal), *Retortamonas* (*Embadomonas*) and *Balantidium*. In addition were found the ciliate of the genus *Troglodytella* and a flagellate of the genus *Hexamita* which are not represented in man. The various combinations of infections in the animals examined are described and the previous records of infections in chimpanzees are discussed. C. M. W.

SASSUCHIN (D. N.). **Hyperparasitism in Protozoa.**—*Quarterly Rev. Biol.* 1934. June. Vol. 9. No. 2. pp. 215–224. With 11 figs. [18 refs.]

In this illustrated article the author reviews our knowledge of parasites which are liable to invade the cytoplasm or nucleus of parasitic protozoa. The importance of these organisms is that on more than one occasion they have been thought to represent stages in the development of the host. It is only by the recognition of their structure and development that such errors are to be avoided. The best known forms are *Sphaerita* and *Nucleophaga*, but others occur such as various microsporidia, while nematodes have even been described as living in ciliates. C. M. W.

RICHARDSON (Flavia L.). **Studies on Experimental Epidemiology of Intestinal Protozoan Infections in Birds.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 373-403. With 1 fig. [25 refs.]

In this long paper the author gives an account of experiments which have occupied him for about 2½ years. They were undertaken to study the susceptibility of young parasite-free chicks to the intestinal protozoa of fowls and other domestic birds and also of a number of wild birds. As was to be expected chicks are readily infected with *Entamoeba*, *Trichomonas* and *Chilomastix* of the fowl. As tested by infectivity to chicks, these protozoa survived in faeces outside the body for 10, 4 and 40 days respectively. The first named survived up to 28 days in diluted faeces, while in this medium the cystless *Trichomonas* survived under an hour. Experimentally infected chicks readily passed on their infection to clean chicks placed in contact with them. Similarly chicks infected from ducks, turkeys and pheasants handed on their infections to healthy chicks associating with them. As regards cysts it was found that the minimum numbers required to produce infections in chicks were 240 for *E. gallinarum* and 1 for *C. gallinarum*. *Trichomonas gallinarum* not possessing cysts required 200,000 trophozoites to infect. The protozoa in wild birds vary in their infectivity to chicks, sometimes heavy infections in the wild bird failing to produce infection in the chick.

The ease with which chicks hand on their infections to one another is of interest from the point of view of the spread of *E. histolytica* infection in families and institutions, and again suggests the importance of food handlers in helping to bring this about [but see this *Bulletin*, Vol. 31, p. 734].
C. M. W.

GUPTA (B. M. Das). **Observations on a Case of Coccidial Infection in Man** (*Isospora belli* Wenyon, 1923).—*Indian Med. Gaz.* 1934. Mar. Vol. 69. No. 3. pp. 133-134. With 2 figs. on 1 plate.

The case is that of a Bengali who had never been out of India. He suffered from acute diarrhoea which gradually subsided during the course of three weeks. A stool examination on the second day revealed oöcysts of the coccidium which were present in fair numbers during the next three days. After this they gradually decreased in number so as to be detectable only by a concentration method. They were last seen on the 20th day. No other cause for the trouble could be discovered.

C. M. W.

RATCLIFFE (H. L.). **Gastric Mucin as a Culture Medium for Intestinal Protozoa.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Feb. Vol. 31. No. 5. p. 602.

Mucin, a natural constituent of the intestinal contents, is prepared commercially as a white powder readily soluble in distilled water, giving solutions which may be sterilized in the autoclave. A 3 per cent. solution of mucin in 0.5 to 0.7 per cent. aqueous NaCl with the addition of sterile rice starch may be used to cover slants (liver infusion agar) or as a liquid medium for the cultivation of intestinal protozoa of various kinds.
C. M. W.

KOFOID (Charles A.), MCNEIL (Ethel) & BONESTELL (Aileen). **Correlation of the Distribution of the Protozoa in the Intestine of *Rattus norvegicus* with the Hydrogen Ion Concentration of the Intestinal Contents and Wall.**—*Univ. California Public. Zool.* 1933. Vol. 39. No. 8. pp. 179–190. With 3 figs. [11 refs.]

The authors have studied the distribution of various flagellates and amoebae in the intestine of rats and have made pH readings of the intestinal contents with a view to determining the range of pH within which these protozoa live.

C. M. W.

KNOWLES (R.) & GUPTA (B. M. Das.). **Some Observations on *Balantidium coli* and *Entamoeba histolytica* of Macaques.**—*Indian Med. Gaz.* 1934. July. Vol. 69. No. 7. pp. 390–392. With 10 figs. on 1 plate.

A species of *Balantidium*, corresponding morphologically with *Bal. coli* of man, is very common in *Silenus rhesus* sold in the Calcutta market. This ciliate has been cultivated in the medium (inspissated horse serum and egg white to which is added a little solid rice starch) recommended for the culture of *Entamoeba histolytica* by DOBELL and LAIDLAW (1926), who also suggested the addition of a few drops of acriflavine solution to keep down the growth of Blastocystis. In most cases excellent results were obtained, the *Balantidium* showing division, encystation, excystation and conjugation. Attempts to infect man with the ciliate failed, though *E. histolytica* of the monkey, which was present in one culture, established itself in the volunteer.

C. M. W.

FISCHER (F. P.) & FISCHL (Viktor). **Elektrophorese von Trypanosomen und Spirochäten. [Electrophoresis of Trypanosomes and Spirochaetes.]**—*Biochem. Ztschr.* 1933. Dec. 27. Vol. 267. No. 4–6. pp. 403–404.

The authors show that trypanosomes and relapsing fever spirochaetes, both in their natural media and in physiological saline solution, whether alive or dead, always make their way to the kathode when brought into an electric field. This property is quite independent of virulence or susceptibility to specific remedies and is the reverse of the behaviour of red blood corpuscles which, as is known, pass to the anode.

C. M. W.

BOXHALL (G. N.), HAPPOLD (F. C.) & LLOYD (LI). **Quinanil as a Bactericidal Agent in the Isolation of an Insect Flagellate.**—*Parasitology.* 1934. Apr. Vol. 26. No. 1. pp. 44–48. [16 refs.]

The authors have succeeded in obtaining bacteria-free cultures of a flagellate closely allied to *Herpetomonas muscarum* from the intestine of *Polytes lardaria* by exposing the flagellates to quinanil in dilutions of 1/10,000 or 1/100,000 for 2–4 hours. Tubes of Locke serum agar containing the same reagent in dilutions of 1/10,000 or 1/50,000 were then inoculated and from these, tubes of Locke serum agar without the reagent. In certain cases cultures of the flagellate were obtained which were proved by exhaustive tests to be free from contaminating organisms. It seems probable that quinanil may be of use for ridding cultures of other protozoa from associated bacteria.

C. M. W.

LWOFF (André). Die Bedeutung des Blutfarbstoffes für die parasitischen Flagellaten. [Significance of Blood Colouring Matter for Parasitic Flagellates.]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Jan. 31. Vol. 130. No. 7/8. pp. 498–518. With 8 figs. [Refs. in footnotes.]

In this highly technical article, which is largely physiological chemistry, the author discusses observations he has made with a view to the determination of the part played by haemoglobin in blood media used for the culture of certain Trypanosomidae. C. M. W.

COLAS-BELCOUR (J.). Influence de quelques bactéries et champignons sur la culture de trypanosomides. [Influence of Bacteria and Fungi on the Cultivation of Trypanosomidae.]—*Ann. Inst. Pasteur.* 1934. May. Vol. 52. No. 5. pp. 533–539.

From the work of LWOFF it is known that *Strigomonas fasciculata* will not grow in peptone water unless some blood, albeit a very minute quantity, is added. The author has found that certain bacteria and yeasts can replace the blood and that they in some way assist the flagellate in its development. Growth of *Leptomonas ctenocephali* could not be obtained under these conditions. C. M. W.

ROBERTSON (Muriel). An *in vitro* Study of the Action of Immune Bodies called forth in the Blood of Rabbits by the Injection of the Flagellate Protozoon *Bodo caudatus*.—*Jl. Path. & Bact.* 1934. May. Vol. 38. No. 3. pp. 363–390. [46 refs.]

With a view to throwing light on some of the problems of protozoal immunity, the author has investigated the production of immune bodies in rabbits by injecting them with bodo, either living or killed by heat or formalin. The paper describes the production of an immune serum, the technique used and the method of cultivating the flagellates.

The heated immune sera tested on living bodos in mammalian Ringer's solution caused varying degrees of immobilization, agglutination and gradual death without lysis. The killing titre of the sera varied from 1/800 to 1/3,200 and it was found that it was better to measure the immune body content by the death of the flagellates rather than by the agglutination, which was more variable. The addition of guineapig complement to the heated sera brought about lysis, which occurred usually before any agglutination became evident. The addition of the complement brought about a reduction in the killing time of the serum dilutions used. Carrying out the tests in distilled water in the place of Ringer's solution it was found that agglutination did not take place though loss of motility and death by lysis occurred. The results obtained in this investigation are discussed and compared with the findings of other investigators who have employed various parasitic protozoa as antigens for the purpose of producing immune sera. C. M. W.

HEGNER (Robert). Passage of *Trichomonas hominis* in a Viable Condition through the Stomach and Small Intestine of a Monkey.—*Jl. Parasitology.* 1934. Mar. Vol. 20. No. 3. p. 199.

Though it has been shown that trichomonas, which, as is well known, form no cysts, are able to withstand the gastric juice and pass through the stomach alive in the case of rats, guineapigs and cats, no one has hitherto shown this to be the case in larger animals. In this note the

author describes how he introduced the trichomonas of man into the stomach of a monkey and later found them alive at various points in the small intestine. The experiment indicates the probability that in man the flagellates may reach the large intestine after ingestion and thus establish an infection.

C. M. W.

HEGNER (Robert). **Infections of the Vagina of Rhesus Monkey with *Trichomonas hominis* from Man.** -*Jl. Parasitology*. 1934. June. Vol. 20. No. 4. pp. 247-248.

Cultures of *Trichomonas hominis* were inoculated into the vagina of *Macacus rhesus*. From a number of experiments it was found that the flagellate was able to survive without multiplication for 20 days. The author and RATCLIFFE have already (1927) described naturally occurring trichomonas (*Trichomonas macacovaginae*) from the vagina of monkeys, while in the following year the author recorded experiments which favoured the conclusion that the intestinal and vaginal trichomonas of the monkey were identical. From the experiments recorded in the present paper it would seem that the human trichomonas is unable to establish itself in the vagina of the monkey. It was found that a half per cent. solution of formalin was completely successful in disinfecting the vagina of naturally infected monkeys.

C. M. W.

LOPEZ NEYRA (C. Rodriguez) & SUAREZ PEREGRIN (Eduardo). **Síndromes parasitarios en la región Granadina y estudio sobre el parasitismo intestinal humano 1. Estudio crítico de los "Chilomastix" parasitos humanos y descripción de una especie nueva hallada en el intestino del hombre en Granada. [*Chilomastix*, Parasite in Man in Granada. A New Species.]**—30 pp. With 3 plates (2 coloured). 1933. Madrid: Comisión Permanente de Investigaciones Sanitarias, Dirección General de Sanidad.

From a study of *Chilomastix* infections of man in Granada the authors arrive at the conclusion that two species occur—the well-known *C. mesnili* and a new one which is given the name *C. granatensis*, which is to be distinguished from the first by its larger size and other details. They also refer to a flagellate described by CHATTERJEE (1923) as *Tetrachilomastix bengalensis*. This was examined by the reviewer, who pointed out that it was a *Chilomastix* (Protozoology, p. 692). The authors of the paper under review, misinterpreting the reviewer's remarks, now, without justification, propose a new name *Chatterjeeia*. Both these names are thus synonyms of *Chilomastix*. Whether the conclusions of the authors that they were studying a new species of *Chilomastix*, their *C. granatensis*, are justifiable or not future investigation alone will show. It should be remembered, however, that *C. mesnili* is subject to great variations in size and that the methods of fixation employed by the authors are open to criticism.

C. M. W.

WATT (John Y. C.). **On *Embadomonas sinensis* Faust and Wassell, 1921.**—*Chinese Med. Jl.* 1933. Nov.-Dec. Vol. 47. Nos. 11 & 12. pp. 1331-1335. With 1 fig.

In 1922 FAUST described as *Embadomonas sinensis* an intestinal flagellate which he had seen in human beings in China. It was stated

to differ from *E. intestinalis* not only in being larger but in that the two flagella were of equal thickness, which was not the case with those of *E. intestinalis*. Some doubt was thrown on the correctness of these conclusions. The author of the present paper records from Peiping two cases of infection with a flagellate corresponding with the form described by FAUST. He is convinced that *E. sinensis* is a good species. It is stated that a dog which showed cysts of *Entamoeba histolytica* in its stools was infected with the flagellate by feeding it with material containing cysts. The appearance of the flagellate three days later coincided with an attack of dysentery associated with the presence of active amoebae. C. M. W.

BISHOP (Ann). **Observations upon *Embadomonas intestinalis* in Culture.**—*Parasitology*. 1934. Apr. Vol. 26. No. 1. pp. 17–25. With 19 figs. on 1 plate. [22 refs.]

The author has cultivated *Embadomonas intestinalis*, the human intestinal flagellate, in a medium consisting of inspissated horse-serum slopes covered either with Ringer egg-white or inactivated horse-serum diluted 1 in 10 in 0.5 NaCl solution. Growth takes place at 17–20°C. as also at 37°C. Attempts to infect tadpoles of the toad (*Bufo vulgaris*) failed. The division stages of the flagellate as seen in culture are described and figured, as also the cysts, in which the nuclear membrane and peripheral chromatin is elongated and stains intensely. The author does not accept WENRICH's contention that the generic name of the flagellate should be *Retortamonas* Grassi, 1879. C. M. W.

ATCHLEY (F. O.) & SWEZEY (W. W.). **A Method for the Enumeration of Ciliate Protozoa.**—Reprinted from *Trans. Amer. Microscopical Soc.* 1934. Jan. Vol. 53. No. 1. pp. 35–39. With 1 fig.

During investigations on ciliates (*Troglodytella* and *Balantidium*) of the intestine of the chimpanzee a method was devised for estimating the total number of organisms in a specimen of faeces within which the distribution is not uniform. STOLL's method for helminthic egg counting was modified for this purpose and was found to give satisfactory results. The procedure is to add 4 cc. of the faecal material to 50 cc. of Ringer's solution to which 6 cc. of a formol iodine fixative has been added. The mixture is shaken up with glass beads, allowed to stand for 24 hours and then reshaken. The ciliates in 0.075 cc. of the mixture are then counted under a 22 × 30 mm. cover slip. C. M. W.

NELSON (E. Clifford). **Observations and Experiments on Conjugation of the *Balantidium* from the Chimpanzee.**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 106–134. With 4 text figs. & 12 figs. on 1 plate. [21 refs.]

A careful study of *Balantidium* from the colony of chimpanzees which had been maintained for over two years at the Johns Hopkins University and its comparison with the ciliates from the pig, guinea-pig and rhesus monkey has shown that it resembles most closely *Bal. coli*, but whether it is actually identical with the form in the pig can only be decided when it has been finally settled whether the *Bal. suis* type which occurs in the pig but not in the chimpanzee is a distinct ciliate

or merely a stage of the *Bal. coli* type. It is concluded that *Bal. caviae* Neiva *et al*, 1914 of the guineapig is a good species. The paper describes the range in size and form of the ciliate of the chimpanzee, the production of the small conjugants and the process of conjugation and the details of nuclear reorganization. The process of endomixis described by CUNHA and MUNIZ (1930) for *Bal. simle* of *Macacus rhesus* is regarded as merely the normal process of macronuclear reorganization after conjugation.

C. M. W.

HERTIG (Arthur T.). **Sarcosporidia in the Myocardium of a Premature Infant. Report of a Case.**—*Amer. Jl. Path.* 1934. May. Vol. 10. No. 3. pp. 413-418. With 1 plate. [23 refs.]

The infant referred to died 26 days after birth, the sarcosporidia being found during the examination of microscopic sections of the heart. As the stage of development of the parasite corresponded with the parasites in experimental sarcosporidiosis of animals on the 26th to 29th day, it is concluded that infection of the infant may have occurred soon after birth.

C. M. W.

MAYER (Martin). Ein neuer, eigenartiger Blutparasit des Affen (*Entopoliypoides macaci* n. g. et n. sp.). [**A New Blood Parasite of Monkey** (*E. macaci*).]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Apr. 5 Vol. 131. No. 3/4. pp. 132-136. With 31 coloured figs. on 1 plate.

In the blood of two Javanese monkeys (*Macaca irus*) the author has encountered a hitherto undescribed parasite in the red blood corpuscles. In the smallest stages it resembles the rings of the subtertian malarial parasite but in the larger forms it is exceedingly irregular in shape and provided with fine processes which terminate in swellings which appear to be attached to the surface of the cell. During the movements of the living parasites these points appear to be fixed. No forms to be distinguished as gametocytes could be detected. There is no pigment in the parasite, which on this account would seem to be related to the piroplasms such as *Babesia avicularis* or *B. decumani*, neither of which, however, is provided with the peculiar knobbed processes. The chromatin in the parasite in Giemsa stained films is in the form of one or two small red granules. Reproduction would appear to be by binary fission. The parasite is readily inoculable from monkey to monkey but not to other animals. Even when the infection is a heavy one it seems to have little effect on the health of its host. On account of its distinctive characters, which are clearly shown in the coloured plate accompanying the paper, the author proposes to name it *Entopoliypoides macaci* n. g. et sp.

C. M. W.

SCHWETZ (J.). Sur la présence de certaines inclusions globulaires dans le sang des cobayes et leur ressemblance avec certaines formes de *Bartonella muris ratti*. [**Globular Inclusions in the Blood of Guinea-pigs resembling *Bart. muris ratti*.**]—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. "No. 6. pp. 515-522. With 2 figs.

The claims of KLEIN, LOPATIZKI and SOLITERMAN (1930) that they had infected guineapigs with the *Bartonella* of the rat, led the author

to repeat the experiments in Stanleyville. He obtained no infection of the guineapigs and suggests that the small coccoid bodies and minute piroplasmalike structures which are known to occur in the red cells of normal guineapigs, particularly young animals, have been misinterpreted as evidence of infection with the rat parasite. Attention was called to the occurrence of these structures in normal guineapigs many years ago by LOW and WENYON (1914) when they were described under the name of *Paraplasma flavigenum* by SEIDELIN, as evidence of the infection of these animals with yellow fever. C. M. W.

KIKUTH (Walter). **The Bartonella and Related Parasites in Man and Animals (Oroya Fever and Verruga Peruviana).**—*Proc. Roy. Soc. Med.* 1934. July. Vol. 27. No. 9. pp. 1241–1249 (Sect. Trop. Dis. & Parasit. pp. 57–65).

This is a general article on the subject of the title, very similar to an earlier one which has been reviewed in this *Bulletin*, Vol. 30, p. 572 and p. 818. In connexion with the therapeutic action of arsenic-antimony compounds on *Bartonella m'ris* infection in rats, it is mentioned that a very potent drug is Std. 386 B, which has the remarkable chemotherapeutic index of 1 : 3,500. [See this *Bulletin*, Vol. 30, pp. 572 & 818.]

C. M. W.

AIR MINISTRY. Medical Notes and First-Aid Treatment for Flights in the Tropics and Sub-Tropics. Promulgated for the Information and Guidance of all concerned. Air Publication 1486. 1st Edition October, 1933.—20 pp. With 3 figs. 1934. London: H.M.S.O. [4d.]

DE GREEF (R.). Note clinique au sujet d'un malade présentant du pian et un goitre concomitant.—*Ann. Soc. Belge de Méd. Trop.* 1934. June 30. Vol. 14. No. 2. pp. 151–152.

KUNDU (M. L.). A Form of Generalized Oedema attended with Malnutrition which is becoming increasingly Common in Rangoon.—*Indian Med. Gaz.* 1934. Aug. Vol. 69. No. 8. pp. 438–440.

MASSIAS (Charles). Deux cas de lithiase biliaire chez des annamites. L'hypocholestérinémie chez les annamites.—Reprinted from *Rev. Méd.-Chirurg. Mal. Foie*. 1934. 8 pp. [15 refs.]

MEDEDEELINGEN VAN DEN DIENST DER VOLKSGEZONDHEIT IN NEDERLANDSCH-INDIË. 1934. Vol. 23. Nos. 2 & 3. pp. 45–110. With 12 figs. on 4 plates. [Refs. in footnotes.]—Jaarverslag van het Geneeskundig Laboratorium over 1933.

NIÑO (Flavio L.) & TRIACA (José Abel). Miasis forunculosa por larvas posiblemente de "*Cochliomya macellaria*."—*Semana Méd.* 1934. Aug. 2. Vol. 41. No. 31 (2116). pp. 336–339. With 5 figs.

PALMER (F. J.). The Acid and Sanitol Treatment of the Intestinal Fluxes.—*Indian Med. Gaz.* 1934. Mar. Vol. 69. No. 3. pp. 137–142.

PORTELLY (J.). Miscellaneous Notes concerning a Partly Developed Region.—*Malayan Med. J.* 1934. June. Vol. 9. No. 2. pp. 49–52.

PRADO (Alcides). Notas sobre o carrapato do chão (*Ornithodoros rostratus*).—*Bol. Biol.* S. Paulo. 1933. Dec. Vol. 1. No. 2. pp. 54–57. With 1 fig.

- PUSA. The Imperial Council of Agricultural Research. Miscellaneous Bulletin No. 1. 45 pp.—List of Publications on Indian Entomology, 1930. (Compiled by the Imperial Entomologist, Pusa.) 1934. Delhi. [As.14 or 1s. 6d.]
- SARNELLI (Tommaso). Primi casi di "Latâh" osservati nell'alto Yemen (Arabia S.O.).—*Arch. Ital. Sci. Med. Colon.* 1934. Oct. 1. Vol. 15. No. 10. pp. 750-759. With 6 figs. English summary (2 lines).
- SEGERDAHL (Elsa). Ein Fall von Hitzschlag während Atropinbehandlung.—*Acta Med. Scandinavica.* 1934. Vol. 83. No. 1-4. pp. 278-280.
- SÉGUY (E.). Destruction des moustiques.—*Ann. d'Hyg. Pub. Indust. et Sociale.* 1934. July. Vol. 12. No. 7. pp. 421-431.
- VENGSAKAR (S. G.), RAGHAVAN (P.) & GODBOLE (G. B.). A Report on the Study of "Blood Pressure" of Indians in Bombay.—*Jl. Univ. Bombay.* 1934. Mar. Vol. 2. Pt. 5. pp. 82-101.
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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.



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[No. 4.

HELMINTHIASIS.

BROWN (Harold W.). **Intestinal Parasitic Worms in the United States. Their Diagnosis and Treatment.**—*Jl. Amer. Med. Assoc.* 1934. Sept. 1. Vol. 103. No. 9. pp. 651-660. With 1 text fig. [34 refs.]

"I shall outline the various treatments that have been found most effective and point out the dangers inherent in such forms of treatment."

Diagnosis is first dealt with, it being pointed out that it is inexcusable to treat for worms without direct evidence of their presence. For microscopic diagnosis the use of several smears and of an examination of a 1 in 20 faecal suspension in saturated salt solution by indirect gravity floatation is held to exclude all, or at least all significant, infections by the common intestinal parasites. "Those interested in diagnosing very lightly infected persons should refer to the method of Lane," the apparatus, however, being held too expensive for the average doctor with only an occasional case to diagnose. [Over 10 years ago the reviewer explained how anyone possessing a centrifuge could use D.C.F. by cheap additions.]

In treatment adequate post-treatment purgation is held of great importance. As to hookworms thymol is dismissed as producing unpleasant symptoms (extreme dizziness and vomiting), oil of chenopodium as occasionally killing in accepted therapeutic doses, betanaphthol for its well known toxicity, carbon tetrachloride for the liver necrosis with occasional death which it causes. The drug of election is tetrachlorethylene in adult dosage of 3 cc.; apparently in contradistinction to the dizziness caused by thymol the giddiness which it produces must not, it is held, be taken as an indication of intoxication but as something to be expected. "Various workers report from 77 to 97 per cent. of hookworms removed by a single treatment." For children and the debilitated, hexylresorcinol may be given in dosage of 0.1 gm. for each year of age up to 10, with 1 gm. as maximum for all ages, which will cure approximately 70 per cent. of cases. [In this dosage LAMSON *et al* reported that the *uncured* as tested by an inadequate diagnostic method were 59 per cent. (this *Bulletin*, Vol. 29, p. 56).]

For ascaris infection hexylresorcinol is given first place with a cure rate of 70 to 80 per cent. after one, and 93 to 98 per cent. after two

treatments. The second place is occupied by oil of chenopodium with a maximum dosage of 1·5 cc., which must be measured by cubic volume and not by drops on account of varying viscosity of various samples. [The essential reason is that drops of the same sample from different droppers vary in size. It is not mentioned that the ascaridole content varies greatly in different consignments, and that in giving any poisonous drug there should be knowledge of the dosage of the toxic principle.] Santonin is given third place with a cure rate of 60 to 80 per cent.

For mixed ascaris and hookworm infections hexylresorcinol is advised on the ground of the reputed cure rates mentioned above: for thread worms hexylresorcinol by mouth and by enema of a strength of 1 in 1,000; for tapeworms, carbon tetrachloride or male fern; for strongyloides, gentian violet; and for trichinella, strong purging to sweep away any adults which may not have penetrated the mucosa.

Clayton Lane.

KELLER (A. E.) & LEATHERS (W. S.). **The Incidence and Distribution of *Ascaris lumbricoides*, *Trichuris trichiura* and *Hymenolepis nana* in Mississippi.**—*Amer. Jl. Hyg.* 1934. Nov. Vol. 20. No. 3. pp. 641-654.

In examining faecal specimens for hookworm ova in Mississippi (this *Bulletin*, Vol. 31, p. 795) the presence of other ova was noted. This report covers ascaris, trichuris, *H. nana* and threadworms.

Since the examination was made by the Stoll-Hausheer method, it may be noted in comment that the true incidence of trichuris ova can certainly not have been disclosed by it. The investigation covered 44,380 whites and 6,353 negroes. The respective positive percentages were, for ascaris 0·9 and 2·5, for trichuris 0·03 and 0·016, and for hymenolepis 0·4 and 0·17; those for enterobius, namely 0·025 and 0·031, do not of course represent the actual incidence. The incidence and intensity of ascaris were highest for both races in children under 10 years old, most infections disclosed less than 10,000 eggs per gram, and they were lighter in whites than in negroes. Moreover, individual counts became greater as the number of infected persons in a family increased. While no study of the environments of these families was made, it is mentioned as proved that this infection is acquired by contamination of hands with soil in which embryonated ascaris eggs are present. Of the 578 specimens in which these eggs were present, they were all unfertile in 277, all fertile in 101, and mixed in 41.

Most of the 17 trichuris cases occurred in places close to sea level with high rainfall. The highest incidence of *H. nana* lay under 10 years of age and is much the same as that discovered by the Rockefeller Sanitary Commission (1910-1914). C. L.

PARDINA (José M.). **Parasitosis apendicular en Córdoba (R. A.). [Parasites in the Vermiform Appendix in Córdoba, Argentina.]**—*Prensa Méd. Argentina.* 1934. Aug. 29. Vol. 21. No. 35. pp. 1635-1640. With 5 figs. [22 refs.]

The author examined 395 appendices removed by operation, 99 from children under 12 years of age, and 296 from adults. Of 99 from children, 39 contained parasites, namely, *Enterobius vermicularis* 38 (in numbers up to 14, female worms largely predominating), and

Trichuris trichiura one. Of 57 removed for acute inflammation 9 contained parasites (15·7 per cent.), while of the 42 chronic appendicitis specimens 30 (71·4 per cent.) showed parasites.

Of the 296 removed from adults 69 (23·3 per cent.) were parasitized. Seventy-two were acutely inflamed and of these 4 (5·5 per cent.) had parasites, whereas of the 224 chronic cases 65 (29·0 per cent.) were so affected. Enterobius was present in 67 of the 69, in numbers up to 27; one showed trichuris, and one fragments of *Taenia saginata* [see also BACIGALUPO, this *Bulletin*, Vol. 27, p. 956]. H. H. S.

VO-VAN (C.). Les helminthiases dans la population infantile de la région provençale. [*Helminth Infection in Children of Provence.*] —*Marseille-Méd.* 1934. May 5. Vol. 71. No. 13. pp. 578–582.

The faeces of 100 children between 2½ and 14 years were examined. Examination of these hospitalized children was in all cases (1) macroscopic, faeces being diluted in normal saline and strained, (2) a squash preparation 50 by 22 mm., (3) a Telemann preparation. The results were:—

	Indigenous.	Immigrants.	Total.
Examined	78	22	100
Parasitized	65	16	81
<i>T. trichiura</i>	65	15	80
<i>A. lumbricoides</i>	8	6	14
<i>E. vermicularis</i>	2	2	4
<i>A. duodenale</i>	1	1	2
<i>H. nana</i>	1	2	3
Unidentified	1	0	1

The histories of the cases of *A. duodenale* infection are given. C. L.

LE MOULT & PIROT. Quelques données statistiques et cliniques sur le parasitisme intestinal des tirailleurs sénégalais en garnison à Toulon. [*Intestinal Parasites of Senegalese Troops at Toulon.*]—*Arch. Méd. et Pharm. Nav.* 1934. July–Aug.–Sept. Vol. 124. No. 3. pp. 342–348.

— & —. Note sur quelques essais thérapeutiques dans l'ankylostomose. [*Treatment in Ankylostomiasis.*]—*Ibid.* pp. 348–351.

A hundred Senegalese admitted to hospital for various complaints had faecal examinations by smear and by certain concentrative methods.

The parasitic findings were:—*E. dysenteriae* 4, *E. nana* 5, *E. coli* 23, *G. intestinalis* 1, trichuris 20, ascaris 9, hookworms 83, strongyloides 4, *T. saginata* 13, *S. mansoni* 13. Judging by egg measurements the hookworms were necators and 20 suffered from definite symptoms.

As to treatment, thymol in average doses of 1·5 grams (22·5 grains) was [naturally] inefficient and its abandonment is accordingly advised. Chenopodium, on an experience of 58 cases, is [unjustifiably] held to be without inconveniences, its ascaridole content is unnoted, it was given

in doses of 1.5 cc. and proved fairly efficient. Tetrachlorethylene on the strength of 8 cases is held to be always efficient in doses of 3, 4 and 5 capsules of unstated size given on three consecutive days. C. L.

- i. VASSILKOVA (Z.); ii. KOROVITSKI (L.) & ARTEMENKO (V.). [**The Rôle of Sewage-Farms in the Epidemiology of Helminthic Infestations.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. [In Russian pp. 149–163; 163–178.]

Two papers devoted to an investigation of the degree of infection with helminth eggs of sewage-farms and the vegetables grown in them.

i. The work was carried out in the outskirts of Moscow. In the water of the sewage collector and irrigation canals eggs of helminths were found per litre as follows. *A. lumbricoides* 700, *E. vermicularis* and *D. latum* 7, *T. trichiura* and *H. nana* 6. In the earth of the beds the eggs of the same forms occurred in smaller quantities, those of *H. nana* and *T. trichiura* being slightly altered. In the sediment obtained by washing vegetables used for consumption in the raw state (lettuce, cucumbers, radishes, tomatoes and cabbage), whether grown on the sewage-farm or exposed for sale in the Moscow markets, there occurred in addition eggs of Taeniids and of Dicrocoelium.

ii. This work was carried out in a sewage-farm of Odessa. The water of the irrigation canals contained 1,428 helminth eggs per 402 litres in the following proportions: *T. trichiura* 1,174, *A. lumbricoides* 217, *H. nana* 23, Taeniidae spp. 2, *Parascaris equorum* 3, *Toxocara mystax* 1, *Toxascaris leonina* 1, *Opisthorchis felineus* 1, Trichostrongylidae and Ancylostomidae 6. Samples of earth contained eggs of the first two only. Insolation causes the degeneration of practically all the eggs contained in the earth to a depth of 2 cm. within 6 days after the irrigation. The number of viable eggs recovered from the vegetables (radishes, green onions, carrots, etc.) was negligible, and it is concluded that sewage manuring is of no epidemiological importance in the spread of helminthic infections in Odessa. [See, however, this *Bulletin*, Vol. 31, p. 611.] C. A. Hoare.

- PODYAPOLSKAYA (V.) & GNEDINA (M.). Sur le rôle des mouches dans l'épidémiologie des helminthoses. [**The Rôle played by Flies in the Epidemiology of Helminthic Infestations.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. [In Russian pp. 179–185. French summary p. 185.]

The authors conducted a series of laboratory and field observations on the part played by the house-fly (*Musca domestica*) and the blue-bottle (*Calliphora erythrocephala*) in the dissemination of the eggs of helminths. In the experimental part flies were allowed to feed during one or two days on human faeces or manure containing the eggs of ascaris, trichuris or diphyllbothrium, either from natural infections or added to the material. Eggs of the first and last, but not of trichuris, were later recovered from the legs and chiefly from the wings of the flies, but none were found on the proboscis. They occurred in large numbers in the droppings of blue-bottles, but not in those of the house fly, probably owing to the fact that the length of the eggs of the helminths used in the experiments exceeded the diameter of the proboscis in the latter insect.

About 2,500 fly droppings were collected on slides scattered in a slaughter-house and a railway dining room, in both of which flies were abundant. In two of the droppings from the abattoir were found eggs of *Dicrocoelium lanceatum*, while in one from the dining room an egg of *Trichuris trichiura* was present. C. A. Hoare.

EGYPT: Ministry of the Interior, Dept. of Public Health. **Sixth Ann. Rep. of the Endemic Diseases Section for 1933** [TOMB (J. Walker), Director].—21 pp. With tables & 1 map. 1934. Cairo: Govt. Press.

I.—ANKYLOSTOMA AND BILHARZIA BRANCH (pp. 1-3).—The numbers treated for hookworm are not stated; it is, however, noted that the distribution of infection among the new patients attending the various branches of the endemic diseases section during 1933 was 164,131. "Only" three deaths were reported from carbon tetrachloride during the year. The use of the drug has been discontinued for trichuris, trichostrongylus, hymenolepis, strongyloides and heterophyes. Of 711,080 persons examined for urinary bilharziasis 58 per cent. were infected; of 685,616 examined for intestinal bilharziasis 23 per cent. were found infected with *S. mansoni*, 2 per cent. with *S. haematobium* and 0.4 per cent. with *E. histolytica*. C. L.

ABDULKADIR-LUFTI. Xanthochromie und Darmparasiten. [**Xanthochromia and Intestinal Parasites.**]—*Deut. Med. Woch.* 1934. Sept. 28. Vol. 60. No. 39. pp. 1472-1475.

The intestinal absorption of lipochrome is increased in various circumstances, the presence of necator and ascaris being the chief of these. C. L.

HALL (Maurice C.). **Principles and Theories of Anthelmintic Medication.**—*Puerto Rico Jl. Public Health & Trop. Med.* 1934. June. Vol. 9. No. 4. pp. 418-433. [Spanish version pp. 434-446.]

"Anthelmintic medication, although in principle and theory analogous to medication in general, deserves more consideration and attention than it has heretofore received. Even now, too little is known concerning long-used remedies and that little is apt to be somewhat vague and empirical."

Five questions are asked and answered. What is the essential factor in successful and safe anthelmintic medication in practice? Good judgment and experience in the physician.

What should the physician know about parasites in order to treat parasitism successfully? The habits and life histories. Thus, ascarids may enter pancreatic and bile ducts and so be unreached by anthelmintic drugs. Hookworm and other larvae may not be in the alimentary canal at the time of deworming, but by reaching it later may cause eggs to reappear in the faeces without post-treatment reinfection. The gravid threadworm leaves the anus to oviposit so that her eggs are rarely found in the faeces.

What should the physician know about anthelmintics in order to use them effectively and safely? The drug to choose in each case, its dose, its effect on the patient, the purgative and its dose. Thus santonin makes ascaris drunk and disorderly, the muscular incoordination being presumably an effect on its central nervous system. *In vitro* experiments to study this have not been made but the results

of such can be transferred to parasitic conditions only with discrimination; thus "if alcohol were an anthelmintic *in vivo* as well as *in vitro* man should have been rid of his worm parasites ages ago." Great stress is laid on purgation in giving post anthelmintic safety; Hall's own theory—he insists that it is theory—is that a purgative by moving the drug along slows absorption and prevents injury from excessive absorption at any particular spot; Glauber's salt is preferred to Epsom salt and it should be one-third saturated. Pretreatment purging is valuable in constipation and where mucus must be removed as in the case of small worms and the small heads of tapeworms, and oils and alcohol should be forbidden before an anthelmintic. A partial removal of worms may have a great temporary clinical value.

"The Stoll egg count has the limitation that while it takes advantage of mathematical probabilities and does so on a very sound basis, this same element of mathematical probability will go against the method when there are very few eggs and large amounts of feces, as a negative egg count under those conditions will not be truly indicative of the absence of egg-producing females. Under such conditions resort must be had to such elaborate methods as the Lane technic, an excellent technic, with the only disadvantage of being somewhat intricate."

Note is made on the possible correlation between chemical structure and anthelmintic efficiency of drugs.

What should the physician know about purgatives? Saline purgatives act rapidly, produce an osmotic flow into the intestinal lumen and so prevent an absorption flow in the opposite direction. If given, castor oil should accompany the anthelmintic.

What should the physician know about the patient? As much about his present state as is necessary before giving any drug, and in particular his habits as to alcohol and fat consumption and pregnancy in the case of a woman.

What should the physician know about prophylaxis? The life history of the parasite concerned. C. L.

TUBANGUI (Marcos A.), BASACA (Mariano) & PASCO (Antonio M.).
Hexylresorcinol as an Anthelmintic: its Efficiency against the Intestinal Parasites of Man.—*Philippine Jl. Sci.* 1934. Aug. Vol. 54. No. 4. pp. 473-481.

The effects on worms and hosts of hexylresorcinol administered to 861 patients in adult dosage of 1.2 gm. in field conditions. Only 381 reported for re-examination.

The drug was given fasting, either in gelatin capsules, which mostly arrived broken, or in sugar coated pills. The purge, when given, was sodium sulphate. The anthelmintic effects were measured by Stoll-Hausheer egg counts once before, and once 10 to 14 days after, treatment and reduced to a "formed basis." [In the case of hookworms and trichuris deworming was not thereby disclosed.] They were as follows:—

Ascaris.—Capsule and purge in 88 cases; percentage of eggs remaining 50, of manifestly uncured 89. Pills without saline in 232 cases; percentage of eggs remaining 18, of manifestly uncured 47. Pills and purge in 61 cases; percentage of eggs remaining 15, of manifestly uncured 36.

Hookworms.—Capsule and purge in 103 cases; percentage of eggs remaining 66, of manifestly uncured 92. Pills and purge in 62 cases; percentage of eggs remaining 26, of manifestly uncured 75.

Trichuris.—Pills without purge in 229 cases; percentage of eggs remaining 72, of manifestly uncured 91. In 46 there were more eggs after than before treatment the greatest difference being 200 per gram. before as against 4,600 after.

Threadworms.—Worms were expelled or symptoms relieved in 13 of 17 cases. In 2 cases enemata of the drug of unstated strength removed great numbers.

Taenia saginata.—In 2 cases tested the head was not passed.

Effects on the host were, in some individuals, slight gastric or intestinal irritation, and transient headache and dizziness. One woman vomited through the nose and has severe burns of the nasal passage. C. L.

MANSON (D.). **A Comparative Record of Anthelmintic Treatment with Tetrachlorethylene and Oil of Chenopodium.**—*Indian Med. Gaz.* 1934. Sept. Vol. 69. No. 9. pp. 500–507.

Four hundred tea garden coolies showed no adverse results from tetrachlorethylene, indeed they enjoyed taking the drug. The anthelmintic effects on hookworms, whipworms and threadworms are reported.

Three dogs having been made completely drunk with 5 cc. of the drug and being quite themselves again in 3 hours, 100 coolies were treated with 4 cc. of tetrachlorethylene shaken up with 2 ounces of saturated solution of magnesium sulphate and given before separation occurred, and showed no toxic symptoms. Accordingly 300 more were divided into 4 nearly equal groups and treated with (group 1) tetrachlorethylene 4 cc., (2)* 3 cc., (3) 3 cc. with oil of chenopodium 1 cc. and (4) oil of chenopodium 3 cc. The incidence of symptoms in each group is tabulated. Here are some of the highest percentage figures: No symptoms (4) 75.00, vertigo (4) 20.83, intoxication (1) 12.5, nausea (3) 6.76, giddiness (2) 12.16, sleepiness (1) 5.0, vomiting (2) 5.41, abdominal pain (2, 3) 2.7, jaundice (3) 1.25.

Evaluation of deworming was by a modification of Stoll's counting method using 0.005 gm. of faeces [so it was not exact for hookworms and whipworms]. So tested, the percentages in which no hookworm eggs were found were (1) 60.00, (2) 44.07, (3) 59.65, (4) 51.61; the corresponding figures for roundworms were 64.61, 55.17, 68.97 and 47.60, and for whipworms 41.3, 35.94, 45.71 and 33.87. The figures are further considered statistically. C. L.

ORENSTEIN (A. J.). [Alleged Dangers of the Administration of Fouadin.] [Correspondence.]—*Jl. Trop. Med. & Hyg.* 1934. Oct. 1. Vol. 37. No. 19. p. 304.

Fouadin should not be given intravenously and daily, but intramuscularly and on alternate days.

Reference is made to CAWSTON's insistence on risk of hepatic damage from fouadin. After mentioning hepatic symptoms following the former method of administration, Orenstein continues:—

"Thereafter all administrations of fouadin were intramuscular and on alternate days. More than 300 school children were treated at various treatment centres organized during school holidays. Not a single case of liver damage was observed in any of these."

"With regard to the efficacy of fouadin as against sodium antimony tartrate, on the basis of the Anti-Bilharzia Committee's experience it can

*The bracketed figures throughout refer to these groups.

be stated that foudadin is approximately as efficacious as the sodium antimony tartrate, provided it is given in proper dosage. Its advantages are relative ease of administration, absence of the danger of local damage associated with intravenous injections of antimony salts, and absence in the majority of cases of any unpleasant by-effects, such as nausea, vomiting, coughing and rigors. Its sole disadvantage, so far as we can judge, is the high cost of the drug.

"In addition to the experience cited above I have had a considerable personal experience with the administration of foudadin, and this taken together with the school treatment centre experience, convinces me that there is no discernible danger of liver damage associated with the proper administration of foudadin."

C. L.

FAKHRY (A.). Antimony Dermatitis treated with Sodium Thiosulphate.
—*Lancet*. 1934. Dec. 22. p. 1394.

Sodium thiosulphate acted rapidly on a case of arsenical dermatitis due to foudadin.

The eruption appeared after the first injection and was aggravated by the second; it lessened after one and disappeared after two intravenous injections of 10 cc. of a 10 per cent. solution of sodium thiosulphate.

C. L.

FAKHRY (Asaad). Tartar Emetic Collapse and Adrenaline.—*Jl. Egyptian Med. Assoc.* 1934. Oct. Vol. 17. No. 10. pp. 851–856.

This collapse is accompanied by a slow weak pulse. Vagus stimulation is suspected as the cause. Adrenalin injection is advocated in treatment and a mixture of tartar emetic with atropine is being tried to prevent it.

C. L.

OESTERLIN (M.) & KRAINICK (H.). Orientierende Versuche zur Chemotherapie der Helminthen. [Trial Experiments on the Chemotherapy of Helminths.]—*Zent. f. Bakt.* I. Abt. Orig. 1934. Aug. 7. Vol. 132. No. 3/4. pp. 222–228.

Seventy-eight chemical substances falling into 10 groups were investigated *in vitro* as to their toxicity to certain helminths, and the results described and tabulated.

Fasciola hepatica.—Of 57 substances tested against the adult flukes, only three showed any efficiency, namely cresyl blue, 3-amino-6-iod-acridine and allyl naphthol. The first was the best, but it had no effect *in vivo*.

Strongyloides stercoralis larvae.—Of 35 substances tried, flavizid and rheonin A, both acridine dyes, proved more effective than gentian violet, a triphenylmethane. Rivanol and tryptaflavine, both acridine dyes, were of little value.

Opisthorchis felineus was very resistant, but among 22 substances tested was injured by phenol derivatives, especially hexylresorcinol.

Schistosoma mansoni was tested as to cercariae against 58 substances, acridine dyes killing them but the complex antimonials failing to do so. The adults were subjected to 14 substances; cresyl blue was effective, so was 3-amino-6-iodacridine *in vitro*, but it failed on mice *in vivo*.

Against *Microfilaria diurna* 15 substances were tried, mostly acridine dyes; only rheonin and flavizid had any effect.

C. L.

HARWOOD (Paul D.). **Effect of Certain Physical Factors on the *in Vitro* Testing of Anthelmintics.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Oct. Vol. 32. No. 1. pp. 131–133.

In vitro tests of drugs against *Ascaris lumbricoides* show that a "liquid excess" of the drug is far more effective than a solid one.

If hexylresorcinol (or certain other drugs) is allowed to stand in contact with 1,000 parts of 0.9 per cent. sodium chloride solution at 37°C., a solid excess will remain. If the same mixture is heated and allowed to cool to 37°C. "the undissolved excess is a supercooled liquid." The latter is far more rapidly lethal than the former to ascaris *in vitro*.

C. L.

LAMSON (Paul D.), BROWN (Harold W.) & HARWOOD (Paul D.). **The Anthelmintic Properties of Certain Alkyl Phenols.**—*Amer. Jl. Trop. Med.* 1934 Sept. Vol. 14. No. 5. pp. 467–478. With 5 charts. [13 refs.]

The result of studies of 4 series of alkyl phenols on ascaris from the pig at 37°C.

"Although we have not yet succeeded in our attempts to find a more practical ascaricide than hexylresorcinol, we have found a number of compounds which act as well *in vitro* and when further tests are made some of them may prove as effective *in vivo*. However, they have the same complicating factor of causing local irritation as hexylresorcinol. It is quite possible, however, that certain of these substances may be so modified that they can be given in a form which will be non-irritating in the mouth yet active on the parasite."

C. L.

BRANDT (W.). Ueber die Wirkung von K pfer auf Eingeweidew rmer. [Action of Copper on Intestinal Worms.]—*Med. Klin.* 1934. Oct. 19. Vol. 30. No. 42. pp. 1399–1400. With 1 fig.

In vitro experiments indicate that cupronat, a copper-containing solution of a strength of 3.5 mgm. per cent., produces tonic contraction of the muscles of ascaris and so will further their expulsion from the intestine.

C. L.

GORDON (R. M.), DAVEY (T. H.) & PEASTON (H.). **The Transmission of Human Bilharziasis in Sierra Leone, with an Account of the Life-Cycle of the Schistosomes concerned, *S. mansoni* and *S. haematobium*.**—*Ann. Trop. Med. & Parasit.* 1934. Oct. 19. Vol. 28. No. 3. pp. 323–418. With 19 figs., 1 diagram, 1 graph and 3 plates (1 coloured). [57 refs.]

Experiments with bred snails show that in Sierra Leone *Schistosoma mansoni* is spread by *Planorbis pfeifferi* and *S. haematobium* by *Physopsis globosa*. The morphology and biology of the immature stages is fully considered.

Of necessity there are details here of purely local importance, but even so their implications are wide. Moreover the case and argument are so closely reasoned that the reviewer finds it impossible to write a satisfying abstract in a reasonable space.

The section on *S. mansoni* points out the evidence that the infection has been introduced only recently from French Guinea [MAASS and

VOGEL, this *Bulletin*, Vol. 28, p. 194], has spread more widely than has been realized, and has been partly controlled by appropriate measures. The highest general incidence occurs in women, for these draw all domestic water and wash all clothes. At Kabala the only snail infected with human type cercariae was *Plan. pfeifferi*; of 1,751 dissected 9.6 per cent. showed cercariae of this type, and experiments on 11 guineapigs and 5 cercopithecus monkeys showed that only *S. mansoni* was concerned. Laboratory bred snails were exposed to attacks of miracidia obtained from this fluke in numbers from 6 to 47 per snail; of 810 *Plan. pfeifferi*, 458 survived for examination, and of 325 tested for cercarial discharge 85.8 per cent. were positive, while of 133 dissected 75.2 were positive; most of the snails lived provided the miracidial concentration of the water in which they were did not exceed 10 per snail and provided the average temperature during development in the snail did not rise above 33°C., so that in the natural conditions locally obtaining most snails will live to discharge cercariae. The authors in parallel experiments failed to infect either *Lymnaea elmetiensis* or *Physopsis globosa* with miracidia of *S. mansoni*. As to ecology the distribution of *Plan. pfeifferi* is very patchy, but most are found in about equal numbers, either on the stream bottom or on the leaves and roots of water plants, particularly of *Acroceras zizanioides* and *Eleocharis fistulosa*; but the clearing of the stream of these plants merely led to a wider distribution of these snails. The temperature associated with the lowest death rate of *P. pfeifferi* lay between 25°C. and 33°C.; if it reached 37°C. all of them died in a few days; they can withstand partial drying for many days, and complete drying for at least 92 hours, if they have learnt to adapt themselves to this, but if the effects of direct sunlight are added they die in a few hours. Breeding probably goes on throughout the year but there is a marked increase of very young forms at the beginning of the rainy season. Full growth is reached in about 6 months and the miracidia of *S. mansoni* show marked preference for half grown forms.

S. haematobium infects 13 per cent. of the inhabitants of Kabala, yet no known snail vector is found in that village—to be precise *Phys. globosa*, an established vector, was not found among nearly 10,000 snails collected. Bred *Plan. pfeifferi* could not be infected with these miracidia, nor could *L. elmetiensis*, but *Physopsis globosa* was so to the extent of 90 to 100 per cent. in small series and of 72.8 per cent. of 262 specimens, and 3 cercopithecus became infected with *S. haematobium* after entry of human type cercariae obtained in one from wild and in two from laboratory bred *Phys. globosa*. Infected *P. globosa* die less readily after infection with *S. haematobium* than do *Plan. pfeifferi* after that with *S. mansoni* (27.5 as against 43.5 per cent.). As to ecology *Phys. globosa* is essentially a bottom and a mud feeder, likes water contaminated with human excreta and is commonest in bathing pools. It withstands a higher temperature than does *Plan. pfeifferi*.

As to the morphology of the larval stages, the miracidia are alike except for the orientation of the 4 large flame cells. In *S. mansoni* their axes lie in the "antero-posterior plane" so that they appear as refractile spheres each containing a flickering cilium; in *S. haematobium* their long axes are "at right angles to this plane" so that they appear as typical long pyramidal-shaped flame cells. The sporocysts, at first motionless besides the tentacles, elongate and become motile and multiply so that 150 have been found in a snail exposed to an average of 10 miracidia. These "type I" sporocysts soon invade the muscles

and finally the liver, become type II motionless, cellular, double outlined and bead-necklace-like, and finally type III with germ balls from which the cercariae develop. A feature, first brought to the authors' notice by Hans VOGEL, is the presence of "tactile hairs" particularly on the anterior and posterior* aspects of the ramus of the tail and on the inner aspects of the furci. The cercarial anatomy is fully described and the authors find no differences at all between those of the two species. Both have 5 pairs of glands.

"The conclusion was reached after the examination of large numbers of cercariae of both species under consideration that there were present two pairs of anterior coarsely granular glands and their ducts which stained selectively with alizarin, and that there were three pairs of posterior finely granular glands and their ducts which stained selectively with lithium carmine or Best's carmine and that neither in the number, situation or reactions of the cephalic glands could the cercariae of *S. mansoni* be differentiated from those of *S. haematobium* as found in Sierra Leone."

In both species the cercariae have 4 pairs of flame cells in the body and 1 pair in the tail and two pairs of ciliated areas in the collecting channels. The existence of the fourth pair in the body of *Cercaria haematobium* is easily overlooked since the 2 pairs in the posterior body overlie one another in dorso-ventral view.

From 50 to 1,000 cercariae may be discharged daily from a snail and the discharge apparently continues as long as the snail lives. As to the effects of temperature, the optimum for rapid development of both species in these particular snails is 32° to 33°C. A drop from 32° to 21°C. increases the duration of the developmental cycle of *S. mansoni* in *Plan. pfeifferi* from 15 to 35 days; and that of *S. haematobium* in *Phys. globosa* from 23 to 67 days; moreover, whereas at 33°C. the migrating sporocysts in *Plan. pfeifferi* could be obtained in tens, at 20°-22°C. they could be counted in hundreds. An appendix describes—methods of transporting live snails and of breeding them; aquaria for incubating infected snails at various temperatures; the media, fixations and stains used in studying the developmental cycles of the worms; the special techniques used; the methods employed to study development in the snails, and methods of mounting adult schistosomes. C. L.

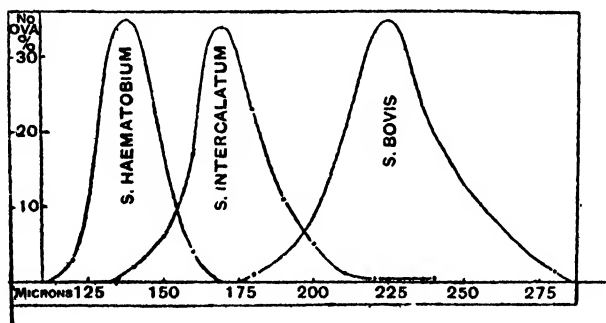
FISHER (A. C.). A Study of the Schistosomiasis of the Stanleyville District of the Belgian Congo.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 277-306. With 1 fig., 3 graphs and 2 plates. [22 refs.]

Intestinal schistosomiasis accompanied by terminal-spined ova occurs in the Stanleyville District of the Belgian Congo [*vide* C. C. CHESTERMAN 1923; this *Bulletin*, Vol. 20, p. 939] and the worms are held to form a new species which is designated *Schistosoma intercalatum*. The work was made possible by a grant from the Royal Society.

There has been unbroken failure to infect *Physopsis africana* experimentally with miracidia from ova passed in the faeces of these infected persons; however, 1 to 3 per cent. of these snails taken from quiet

*Evidently ventral and dorsal which will then be the meaning of the terms used for the miracidial flame cells. The authors write that these hairs "do not appear to have been recorded hitherto." TAKAHASHI, however [this *Bulletin*, 1928, Vol. 25, p. 950], writing on the cercaria of *S. japonicum* says—"There are certain numbers of sensory organs (a process with a delicate hair) on the surface of the body and tail." They are figured in the Japanese version of the paper.

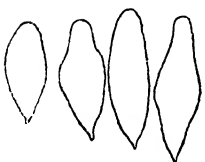
river reaches give off "human bilharzia cercariae," and with these mice and a sheep have been infected. The descriptions of the adults are given with the comment that "none of the morphological characteristics of this parasite, apart from the ovum, are such as to enable it to be differentiated clearly from either *S. haematobium* or *S. bovis*. The size of mature intrauterine ova averages 130 by 40 μ , while those in faeces in man and experimental animals measure 140 to 240 μ by 50 to 85 μ with an average of 175 by 60 μ . As to shape, "eggs of the short, squat variety may readily be confused with those of *S. haematobium*, though as a rule, a distinction can be made by the more rounded extremities of the last-named species. On the other hand long spindle-shaped eggs may strongly resemble those of *S. mattheei*



Length-frequency curve for mature ova of *S. intercalatum*, from human faeces, compared with approximate frequency curves for *S. haematobium* and *S. bovis*.



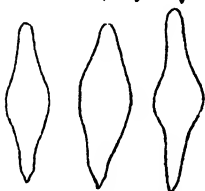
Mature ova of *S. haematobium*.



Mature ova of *S. intercalatum*.



Intra-uterine ova from several female *S. intercalatum*.



Mature ova of *S. bovis*.

A comparison of the shape of ova of *Schistosoma intercalatum* with those of *S. bovis* and *S. haematobium*.

[Reproduced from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*.]

or *S. bovis*, but these ova never reach such large dimensions as in *mattheei* and *bovis*." The spine may attain a length of 20 μ ; "this usually serves to distinguish it from *S. haematobium*."

No natural hosts other than man have been found. The shortest interval after exposure to infection in which ova appeared in the faeces of mice was 41 days. Spinster worms are short and flattened and may have incurred edges reminiscent of the male, and while still fresh a few scattered cuticular bosses; the acetabulum is markedly developed. Since Fisher has found a single pair of coupled worms surrounded by ten spinsters and has never found a wedded female unless attended by her mate he notes this steadfast monogamy and believes with BRUMPT that the female does not leave her mate for oviposition. [As CAWSTON has repeatedly insisted, gravid female worms are easier to kill than males. Are spinster females with their male characters also resistant to poisoning, and can re-appearance of eggs after drugging be due to surviving males taking up with surviving spinsters?]

This intestinal infection occurs in villages for 100 miles along the Congo from the Stanley Falls down to the mouth of the Lomami River and has also been found in a child from Bengamisa 50 miles up the Lindi River which flows into this stretch of the Congo from the north. The snails are found in thousands in quiet shady stretches of the river which are used as latrines by villagers and boatmen. If they have been shedding cercariae for long they become covered with a brown slime. The swimming and penetration movements of the cercariae are described. "It is commonplace to see one man bathing a few feet from the bank, with another easing himself into the water not far upstream" and since washing is constant, opportunities for infection are many.

Sigmoidoscopy shows lesions from the anus to the pelvi-rectal junction and none higher, and the prevalent symptoms are dysentery and abdominal pain; but CHESTERTON is of opinion that the infection is an important factor in causing an atypical pneumonia commonly encountered here. The infection is one of the young, examinations giving uniformly negative results in those over 30 or 35. Acriflavine was used by mouth in a 2 per cent. solution given in 5 equal daily doses with a total of 0.01 gram per kilo. Symptoms ceased within 48 hours. In 49 cases all but 6 showed no ova, or in 4 cases only degenerate ova, by the time the course was complete; the 6 were quite uninfluenced. Of the 43, 34 were followed up and half showed reappearance of ova. Proflavine gave comparable immediate results in 7 cases, and 2 which were followed up were negative 3 months later. The difficult problem of control is discussed.

C. L.

CONNOLLY (M.). On the Planorbid Hosts of Bilharziasis in South and West Africa.—*Ann. Trop. Med. & Parasit.* 1934. Oct. 19. Vol. 28. No. 3. pp. 439-443. With 12 figs.

Extreme variability of certain species of the red-blooded snails belonging to *Physopsis* and *Planorbis* renders it likely that for medical men the exact trivial name of a local race is of less importance than an old and possibly over-comprehensive one.

Planorbis pfeifferi Krauss, 1848 is the oldest name applied to nearly-allied members of the genus south of Egypt. It attains fairly large

dimensions (15 by 6½ mm. in major diameter and thickness) with 5 slowly increasing whorls; the aperture is not noticeably larger than the whorl to which it forms the end, and is normally on the same plane with it, though it may incline a little above or below it. It inhabits the greater part of the continent south of the Kunene and Zambesi rivers, but Connolly has noted typical shells from Kenya and Northern Nigeria. Certain specimens from Kabala were submitted to Louis GERMAIN of Paris who reported that they were without question a form of *P. bridouxii* Bourquignat, a synonym of *P. stanleyi* Smith 1888, but that the two forms are closely allied and that "the conclusion is that your *Planorbis* from Sierra Leone is evidently near to *pfeifferi* Krs., but still more so to the forms from L. Chad of *bridouxii*, Bgt., and it seems more suitable to classify it as this species." WATSON reports after a study of the anatomy that the central tooth of the radula differs in a minute detail, exhibiting in 4 dissected snails a small narrow median denticle between the two larger cusps which is held to entitle "*Plan. bridouxii*" to specific rank [GORDON, DAVEY and PEASTON note (p. 237 above), that these differences, recognizable only by an expert, entitle them to continue to use the name familiar to medical men]. As to the difference between *Physopsis africana* Krauss, 1848 and *Ph. globosa* (Morelet), 1866, Connolly writes:—"When describing this species [*P. globosa*] Morelet rightly stressed the fact of its slight rimation, which affords the only real and fairly constant point of difference between itself and *africana*." [In other words it seems that the individual shell cannot always definitely be assigned to either species, so that the medical man need not be too anxious about the distinction.] C. L.

VAN DEN BERGHE (Louis). Les schistosomiasis humaines et animales au Katanga (Congo Belge). [**Human and Animal Schistosomiasis in Katanga.**]-*Ann. Soc. Belge de Méd. Trop.* 1934. Sept. 30. Vol. 14. No. 3. pp. 313-371. With 5 figs. & 15 plates. [30 refs.]

It is felt that in the Belgian Congo, which comprises the greater part of Central Africa, schistosomiasis has not yet been systematically considered; hence this study.

During the last 10 years the reported cases of schistosomiasis have steadily increased. Keys of the subfamilies and genera of the Schistosomidae are given. Twelve species are considered of which only 4 (*S. haematobium* and *S. mansoni* of man and *S. bovis* and *S. margrebowiei* of animals) are held to have distinctive characters. Of *S. faradiei* Walkiers, 1928 only the eggs have been described and that without measurements; the separation of *S. mattheei* from *S. bovis* is not admitted by all. *S. spindalis africana* A. Porter, 1929 is based on shape of egg and size of cercaria, both points difficult of exact determination. *S. curassoni* seems to be *S. bovis* and *S. rodhaini* to be a variety of *S. mansoni* in an abnormal host. *S. intercalatum* Fischer, 1934 is not sharply defined from *S. haematobium* and *S. bovis*. There are dealt with the known local habitats of *Planorbis adowensis*, *P. sudanicus*, *Physopsis africana*, *Bulinus forskalii*, *Limnaea natalensis*, *Melanoides crawshayi* and *M. mweruensis*, the effect of season, the percentage of infected molluscs their cultivation and egg laying. Human infection is considered medically and hygienically. C. L.

GAUTHIER (Henri). Enquête sur la répartition en Algérie des mollusques susceptibles de véhiculer la bilharziose vésicale. [**Distribution in Algeria of Potential Mollusc Carriers of *S. haematobium*.**]—*Arch. Inst. Pasteur d'Algérie*. 1934. Sept. Vol. 12. No. 3. pp. 305–350. With 1 map & 9 figs. on 3 plates. [17 refs.]

Bulinus is disappearing in Algeria.

At the end of a survey of local importance and value it is pointed out that acid waters do not harbour this snail, alkaline waters do so here and there but less so than formerly as they are modified by man. Only Lake Onbeira seems likely to be too big to attack economically. C. L.

PALLARY (Paul). Enquête sur les bullins en Algérie. Le marais d'en Naro (dép. d'Oran), de formation récente. [**Inquest on the *Bulinus* of Algeria. The En Naro Marsh.**]—*Arch. Inst. Pasteur d'Algérie*. 1934. June. Vol. 12. No. 2. pp. 255–258. With 1 fig.

No molluscs are found in this swamp, which the author states is of quite recent formation. A. G. B.

GOBERT (E.). Note sur la bilharziose en Tunisie. [**Schistosomiasis in Tunis.**]—*Arch. Inst. Pasteur de Tunis*. 1934. Aug. Vol. 23. No. 3. pp. 348–359. With 4 plates (1 map).

Infection by *S. haematobium* through *Bulinus contortus* was investigated at Gafsa and El-Oudiane.

Gafsa.—Percentages infected as ascertained by centrifuging urine were : men 74, women 38·5, boys 58·2, girls 73·4. Where the temperature of water collections, was 27°C. or less *B. contortus* was present ; where 28° or over it was absent. The percentage of snails with bilharzial cercariae varied from 0 to 65.

El-Oudiane.—Percentages of children infected varied from 0 to 100 ; only 9 adults were examined and from one locality only ; all were infected. Temperatures of 19 water collections varied from 18° to 29°. The only 3 with infected snails had temperatures of 19°C. C. L.

ANDERSON (Ch.) & GOBERT (E.). Note sur la présence, en Tunisie, de *Schistosoma bovis*. Infection naturelle de *Bulinus contortus*. [***Schistosoma bovis* in Tunis conveyed by *B. contortus*.**]—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 850–852.

Furcocercous cercariae in *Bulinus contortus* in the Mediterranean basin do not necessarily imply infection with *S. haematobium*.

Anderson and Gobert having pointed out that when seeking for haunts of *B. contortus* carrying human furcocercous cercariae they came across these snails infected with *S. bovis*, Professor BRUMPT in discussion pointed out that in 1929 he showed that this trematode and snail were associated in Corsica. [The full description of BRUMPT's convincing series of experiments is found in *Ann. Parasit. Humaine et Comparée*, 1930, Vol. 8, pp. 17–50.] C. L.

VIGLIETTA (Carlo). Ricerche sulla diffusione della schistosomiasi vescicale fra i bambini indigeni di Derna. Misure profilattiche adottabili. [**Urinary Schistosomiasis among Children in Derna. Prophylaxis.**]—*Arch. Ital. Sci. Med. Colon.* 1934. Oct. 1. Vol. 15. No. 10. pp. 760–766. [10 refs.] English summary (3 lines).

The oasis of Derna (Cyrenaica) has been reputed as a focus of *S. haematobium*. The author examined 606 children attending the elementary schools ; after centrifuging the urine in each case he found

9 only infected, 1·4 per cent. *Bulinus contortus* is present in the district. For prevention he recommends the usual measures of treating the infected with foudadin, or emetine, destroying the snail with copper sulphate, 5 parts per million, and educating the inhabitants as to methods by which infection is contracted and how to avoid it.

H. H. S.

BARSOU (H.). **The Bilharzial Appendix.**—*Jl. Trop. Med. & Hyg.* 1934. Dec. 15. Vol. 37. No. 24. p. 387.

Schistosomes do not cause appendicitis.

Of 53 appendices thoroughly examined histologically after removal for appendicitis, 19 per cent. showed schistosome eggs. Of 46 appendices taken from bodies dying of different diseases, 28 per cent. showed these ova. The population of Egypt is heavily infected with these parasites, but appendicitis among them is rare.

C. L.

LOWENTHAL (H. F.) & ROBERTS (R. A.). **Bilharzia Affecting the Left Ureter Primarily.**—*Lancet.* 1934. Sept. 29. pp. 706–707. With 1 fig.

A report from Kimberley of a greatly thickened ureter which after removal was shown to be bilharzial and which had caused for 12 months occasional pain on micturation with haemorrhage. These ceased after the kidney and ureter had been removed. Tartar emetic was then given.

C. L.

FAUST (Ernest Carroll), HOFFMAN (William A.), JONES (Charles A.) & JANER (José L.). **Studies on Schistosomiasis Mansoni in Puerto Rico. II. The Epidemiology and Geographical Distribution of Schistosomiasis Mansoni in Puerto Rico. 2. A Survey of Intestinal Parasites in Endemic Schistosomiasis Areas in Puerto Rico.**—*Puerto Rico Jl. of Public Health & Trop. Med.* 1934. June. Vol. 9. No. 4. pp. 447–471. With 1 map. [40 refs.] [Spanish version pp. 472–491.]

“Data are presented on the protozoan and helminth infections of representative cross sections of the Puerto Rican population, based on single specimen examinations of 1,003 persons.”

Each specimen was examined, within 24 hours or after standing in a refrigerator, by 3 methods, one diluted in physiological salt solution, one stained with Donaldson's iodine and one an iodine-stained centrifugal precipitate, all being covered preparations.

“The percentages actually found in the Puerto Rican survey are as follows:—*Endamoeba histolytica*, 14·5; *E. coli*, 34·2; *Endolimax nana*, 16·3; *Iodamoeba bütschlii*, 3·5; *Giardia lamblia*, 14·3; *Chilomastix mesnili*, 0·7; *Balantidium coli*, 0·2; *Ascaris*, 9·9; *Necator* (and *Ancylostoma*), 33·5; *Trichocephalus*, 44·6; *Strongyloides*, 4·6; *Enterobius*, 0·4; *Schistosoma mansoni*, 12·2 and *Hymenolepis nana*, 0·1. The percentage of positive cases was 81·2; the protozoan index, 0·84; the helminth index, 1·05, and the total parasite index, 1·89. These totals are lower than those computed for Colombia (single examination) and Panama (2–3 examinations), and are higher than those for New Orleans (2–3 examinations) and Tennessee (single examination).

“The incidence of *Schistosoma mansoni* (12·2 per cent.), as indicated by this survey, is believed to constitute a fair estimate of this infection for Puerto Rico, although its actual distribution is ‘spotted,’ and depends on

factors which are essentially independent of those controlling the other parasites found on the Island."

[This is a continuation of the paper abstracted in Vol. 31, p. 777.]

C. L.

FAUST (Ernest Carroll) & HOFFMAN (William A.). **Studies on Schistosomiasis Mansonii in Puerto Rico. III. Biological Studies. 1. The Extra-Mammalian Phases of the Life Cycle.**—*Puerto Rico Jl. of Public Health & Trop. Med.* 1934. Sept. Vol. 10. No. 1. pp. 1-47. With 2 text figs. and 6 plates (1 coloured). [44 refs.] [Spanish version pp. 48-97.]

After mentioning the historical background and describing the methods used in the investigation, the life history of *S. mansonii* outside the definitive host is detailed and there are described 3 other cercariae found in the snail concerned, all new, under the names of *Cercaria neotropicalis*, *C. marini* and *C. paucispina*.

As to methods of staining, brilliant cresyl blue was used *intra vitam* for second generation sporocysts and for cercariae, while miracidia and cercariae after fixing in Bouin's fluid were stained with Bullock's haematoxylin.

Faecal eggs are most consistently viable in semiliquid stools passed during early stages of infection; but in such stools the enclosed embryo lives barely 24 hours at temperatures of 75° to 90°F. though in formed stools they survive for 2 or 3 days. In formed stools at 45° to 50°F. they live for a week or more with apparently unimpaired vitality. Urine is very toxic. Hatching is apparently caused by osmotic pressure produced by entry of water, and is slow, for most miracidia have not hatched after 16 hours in water. After throwing off the vitelline envelope the miracidia are found mostly in the top inch and bottom half inch of the water, and rarely survive for 24 hours.

The valid name of the Porto Rican intermediate host is, it is claimed, *Australorbis glabratus*, and not *Planorbis guadeloupensis*. As to the specific name, *guadeloupensis* Sowerby, 1821, must give place by priority to *glabratus* Say, 1818. As to the generic name, *Planorbis sensu stricto* applies only to European species, the American forms belong to *Helisoma* Swainson, 1840. But *Helisoma* has been divided into several sub-genera, of which *Planorbina* Dall, 1905 contained *glabratus*. But the subgeneric name *Planorbina* was preoccupied by HALDEMAN in 1842 so cannot be used for this group, and was therefore superseded by PILSBRY in 1934 by the name *Australorbis* which is held to require full generic rank, with *glabratus* as type. The anatomy of this snail is described. The miracidia attack the tentacles and head-foot organ. The earliest sporocysts were seen on the 8th day, they grow little till they have travelled to the lymph spaces round the digestive gland and reach 1 mm. in length on 12th to 15th days. Secondary sporocysts break out about 5 days later and cercariae from them have appeared by the 23rd day, bursting out as mature from the 22nd to 28th days and thereafter continuing to be discharged. In 4 snails the number of cercariae discharged after infection by a single miracidium varied between 75,000 and 210,000, the last snail still discharging 2,500 of them daily when the observation ended. There may be a high mortality among infected snails; indeed if the rupture in the tunica propria made by the cercariae is large the snail may bleed to death in a few minutes.

The sporocysts and cercariae are described, and it is insisted with the emphasis of italics that the latter have 6 pairs of glands, 2 anterior large granular and oxyphilic, and 4 posterior fine granular and basophilic. "It seems likely that observers who have failed to find the complete number of glands in mature cercariae have not been able to demonstrate one posterior pair which, on ventral or dorsal view, is almost always masked by another similar gland at this same level." This conclusion is supported by figures of glands in immature cercariae.

Cercariae escape from the snail between 9 a.m. and 2 p.m. They do not remain on the surface, and are easily transported by currents; 95 per cent. are alive after 24 hours, less than 10 per cent. after 30, which allows 2 middays for possible entry into man. C. L.

EISBACH (L.). De chirurgische beteekenis van de darmafwijkingen bij Bilharzia Mansoni in Suriname. [*The Surgical Manifestations of S. mansoni in Surinam.*—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Sept. 25. Vol. 74. No. 20. pp. 1261-1276. With 8 figs. on 4 plates. English summary.

The author's classification of these follows no fixed rule, being partly on pathological lines, partly on the site of lesions. Thus, he mentions three forms of colitis—catarrhal, sclerosing and polypoid—and a subperitoneal, omental and appendicular bilharziasis. Secondary infection may complicate the picture by causing further infiltration, abscess formation and perforation. In the sclerosing form treatment by enterostomy has proved successful. In spite of the frequency of this form of schistosomiasis in Surinam the author cannot find evidence that there are any grounds for the widespread belief that malignancy may develop as a complication of the lesions set up. The paper is illustrated by 8 excellent photographs of the associated pathological conditions. H. H. S.

BOURGUIGNON (G. C.). Les réactions cellulaires tumorales dues à *Schistosoma mansoni* dans le grand épiploon de l'homme. [*Cellular Reaction in Swellings due to S. mansoni in the Great Omentum.*—*Ann. Soc. Belge de Méd. Trop.* 1934. Sept. 30. Vol. 14. No. 3. pp. 257-261. With 6 figs. on 3 plates.

Surrounding eggs in the great omentum there occur pseudotubercles with fibroblasts, giant cells and an onion-like fibrosis. C. L.

BEQUAERT (J.). The Molluscan Intermediate Host of the Blood Fluke, *Schistosoma japonicum* Katsurada, in the Philippines. With a Note on the Genus *Blandfordia* by H. A. PILSBURY.—*Jl. Parasitology*. 1934. Sept. Vol. 20. No. 5. pp. 280-284.

Strong reasons are given for simplification of the nomenclature of the snails which carry *S. japonicum*.

Bequaert is forced to conclude that *Oncomelania hydrobiopsis* is a synonym of *Blandfordia quadrasi* and that *Oncomelania*, *Hyposobia*, *Hemibia* and *Katayama* are synonyms of *Blandfordia* A. Adams, 1863. He adds "It would seem that the smooth-shelled Oriental Amnicolidae known to act as intermediate hosts of the blood fluke, *Schistosoma japonicum*, such as *nosophora* Robson, *formosana* Pilsbry and Hirase, and *quadrasi* Möllendorff, should all be placed in the genus *Blandfordia*. The ribbed-shelled species, *hupensis* Gredler, may be

left in *Oncomelania*, if one wishes to retain that name in a generic or subgeneric sense." Pilsbry adds that, since *Katayama* is a synonym of *Blandfordia*, it appears that possible *Schistosoma* hosts occur over all Japan, since *Blandfordia* is found as far north as Yesso. C. L.

LI (Fu-ching). Beobachtung ueber die Biologie von *Oncomelania*, des Zwischenwirtes von *Schistosoma japonicum* in China. [Biology of *Oncomelania*, the Intermediate Host in China of *S. japonicum*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Dec. Vol. 38. No. 12. pp. 519-524. With 2 figs.

A note on the development of this snail and the conditions necessary for this, particularly the vegetation and the state of the bottom.

C. L.

MADRAS: Ann. Administ. Rep. of the Civil Veterinary Dept. for 1933-34 [SAUNDERS (P. T.), Director].—55 pp. With 2 plates. 1934. Madras: Govt. Press.

SCHISTOSOMES IN PIGS (p. 34).—This report suggests that in spite of conclusions to the contrary there is in India no schistosome parasitizing man. The ova in question probably came from pig's faeces.

"In the pig, hitherto, only one kind of schistosome, viz., *S. japonicum*, Katsurada, 1904 has been recorded in the Far East, and the finding of this new species in the pig in Madras is of some interest. In 1906 Chandler, while working on the prevalence and epidemiology of hookworm and other helminthic infections in India, wrote a paper on a new schistosome infection in man. He saw schistosome ova in some samples of faeces collected from defaecation areas to which pigs had access in two villages in North Bengal. Chandler assumed the faeces from which he got the samples were passed by human beings, because of the nature of stools and the presence of ova of hookworms, *Ascaris* and *Trichuris*, but for obvious reasons, these facts do not prove the correctness of his assumption. Although nothing was known of the adults for convenience of reference, he named this apparently new species *Schistosoma incognitum*. The fact that these ova resemble those obtained in the schistosomes from pigs here, suggested the probability that the faeces in which he saw them were from pigs that had access to the defaecation areas and not from human beings. Up to the present time, there is no evidence to show that any new schistosome has been found in man in India other than those found in people after residing in endemic areas of *S. mansoni* and *S. haematobium*. Hence it is possible to assume that Chandler saw these ova in the sample of faeces of the pig, the adult of which has now been described and the name "*Schistosoma suis*" has been suggested for it."

[The description of *S. suis* does not appear in the report and has not been traced. For the reference to *S. incognitum* see this *Bulletin*, Vol. 24, p. 174.]

C. L.

- i. EL DIWANY (M. A. El Moneim). **Acriflavine for Schistosomiasis.** [Correspondence.]—*Lancet*. 1934. Sept. 8. pp. 571-572.
- ii. KHALIL (M.) & SALAH (M.). **Treatment of Schistosomiasis with Acridine Compounds.**—*Ibid.* Oct. 20. pp. 862-863.
- iii. FISHER (A. C.). **Acriflavine for Schistosomiasis.** [Correspondence.]—*Ibid.* Nov. 3. p. 1017.
- iv. KHALIL (M.). **Acriflavine for Schistosomiasis and Ankylostomiasis.** [Correspondence.]—*Ibid.* Nov. 24. p. 1193.

These reports follow Fisher's note on the treatment of schistosomiasis with acriflavine [this *Bulletin*, Vol. 31, p. 775].

i. A distinction is drawn between yellow trypaflavine with a formula of 3 : 6 diamino-10-methylacridine chloride, and brick-red acriflavine with one of 2 : 8 diamino-10-methylacridine chloride. Acriflavine has been used, and well borne, by mouth and anus. An editorial note points out that the two substances are identical, confusion having arisen because two systems of numbering have been adopted to indicate the positions of substituted groups in the acridine molecule. Variations in colour may be due to the fact that commercial samples consist of a mixture of varying proportions of the hydrochlorides of diamino-methyl-acridine-chloride and diamino-acridine.

ii. Fisher is stated to claim that schistosomiasis can be cured in 5 days by acriflavine, which is a synonym of trypaflavine. Treatment of 81 cases with acridine derivatives has shown no curative effect on either *S. haematobium* or *S. mansoni*. The treatment used consisted of : trypaflavine orally in solution or capsules, or intravenously ; diamino-methyl-acridine in capsules ; and atebirin in tablets by mouth. Erythema of the face with peeling was apt to occur, as did vomiting with the bigger doses (0.5 gm. daily) ; a few developed diarrhoea and a few collapsed. In 3 cases after 4 gm. of the drug a galactose liver test showed no impairment of function. Cercariae of *S. mansoni* lived for 3 hours in a trypaflavine solution in dilute serum.

iii. Fisher points out that Khalil's statement that he claimed cure in 39 of 52 cases is incorrect. Owing to the short observation period he was at pains to avoid any claim to a cure. It has been possible to keep 34 cases under observation for 3 to 6 months. Ova have reappeared in half, the other half are free from ova or symptoms. Most of the cases carried heavy infections. He is at a loss to explain the discrepancy between the two series.

iv. Khalil reports chemical analyses indicating that English preparations are the hydrochloride. Reports on 4 cases indicate that trypaflavine has no anthelmintic effect on ankylostomiasis [that is, the locality being Egypt, on ancylostomiasis]. C. L.

VAN NITSEN (R.). Traitement de la bilharziose intestinale par la fouadine concentrée. [Treatment of Intestinal Schistosomiasis by Concentrated Fouadin.]-*Bull. Méd. du Katanga*. 1934. Vol. 11. No. 4. pp. 123-124.

A calcium salt is concerned instead of a sodium one as in ordinary Fouadin, and 1 cc. contains 14.3 mgm. of antimony III [? trivalent] instead of 8.5 mgm. The injections at 24-hour intervals consisted of 1 cc., 2 cc. and thereafter 3 cc. In 13 cases eggs disappeared as follows :—after 1 and 2 injections, once each ; after 3, three times ; after 4, twice ; after 5, twice ; after 6, four times ; after 9, once. Abdominal pain and bloody stools were the rule after treatment began.

C. L.

SALAH (M.) & HASSAN (A.). The Action of Antimony on the Liver with Special Reference to its Use in the Treatment of Schistosomiasis.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Jan. Vol. 39. No. 1. pp. 1-14. [31 refs.]

In bilharzial cases antimony does not damage but rather improves liver function.

Cases were treated either with foudadin or tartar emetic. As to foudadin, a man of 60 kgm. received as first dose 3.5 cc. and thereafter 5 cc. ; the first 3 injections given daily, the rest every other day ; the course covering 9 injections, or more if eggs had not by then disappeared. Tartar emetic was given similarly, the first dose being 1 cc. of a 6 per cent. solution, the others 2 cc.

Of 23 cases with clinically normal livers, 8 showed disturbed liver function, mainly glycogenic, before treatment and only 2 after it. Of 20 cases with clinically enlarged or cirrhotic livers, 7 showed positive galactose tests before treatment and only 3 after it.

Of 28 cases of jaundice, 15 of whom had a previous history of a tartar emetic course, 22 cases were improved or cured ; 19 of them had active schistosomiasis, and the rate and degree of improvement were greater in the bilharzial than in the non-bilharzial group. Accordingly it is concluded that antimony had not disturbed liver function in these cases ; nor in 6 followed for varying periods up to one year was there any evidence of delayed action.

C. L.

BARNEOUD (Jean). Le traitement de la bilharziose vésicale par le Dn 7 et le Dn 18. [**Treatment of Vesical Schistosomiasis by Dn 7 and Dn 18.**—*Bruxelles-Méd.* 1934. Dec. 9. Vol. 15. No. 6. pp. 166-170.]

These trivalent antimonials have produced excellent parasitocidal effects on *S. haematobium*.

Five patients were treated with Dn 7 and 8 with Dn 18. In all of them repeated examinations over 3 months have shown absence of eggs. The sequelae have been cough and vomiting and are spoken of as very rare and very benign. A case is, however, mentioned, apart from these 13, in which intravenous injection of 0.4 gm. of Dn 18 produced laryngeal spasm, with sensations of constriction of the chest and suffocation, and with a small pulse of 120 ; gluteal intramuscular injection of 0.15 gm. of Dn 7 produced local pain and trouble in walking, and intravenous injection of the same produced vertigo with cold sweat, cough, vomiting and rapid pulse, so that the treatment was abandoned. The doses advised for Dn 7 are of 0.25 gm. first every other day and then daily intravenously with a total varying from 3 to 4.15 gm. ; of Dn 18 the doses are 0.4 gm. with a total of 3 to 5.6 gm. over an average period of 15 days. The drugs are produced by the Union Chimique Belge.

C. L.

CAWSTON (F. G.). **Evidence of the Successful Destruction of Schistosomes.**—*Parasitology*. 1934. Oct. Vol. 26. No. 4. pp. 460-462.

Absence of eggs does not imply absence of or cure of schistosome infection.

Cawston returns to the persistence of male parasites after treatment which has killed females, or the possibility of a slow development of the latter, and points out the likelihood of missing faecal or even urinary ova. He draws attention to complement fixation tests and to persistent eosinophilia or a rise in its incidence during treatment as indicating

presence of parasites. He suggests that shoulder pains are hepatic in origin and that investigation is needed to determine whether they are antimonial in origin or due to poisoning of parasites. C. L.

- i. OESTERLIN (M.). Zur Chemotherapie der experimentellen Schistosomiasis. [Chemotherapy of *S. mansoni* and *Opisthorchis* Infection.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Oct. Vol. 38. No. 10. pp. 433-441. [19 refs.]
- ii. ———. Zur Chemotherapie des Katzen-Leberegels (*Opisthorchis felineus*).—*Ibid.* pp. 441-445. [13 refs.]

i. Experiments on mice suggest the discovery of a new drug active against *S. mansoni*.

Sixteen drugs were tested and of these Sdt. 386 B gave promising results. It is a brown powder containing 18 per cent. of arsenic and 20 per cent. of antimony, and was used in a dose of 0.15 gm. per kgm. As to the transference of results to man it is necessary to add that in these mice tartar emetic was of little value. Other drugs proved valuable vermicides but unfortunately too little selective, killing tissues at the site of injection. The value of Sdt. 386 B was confirmed on a monkey.

ii. Sdt. 386 B. proved effective in opisthorchis infection of cats in a dose of 20 mgm. per kg. C. L.

HASSAN (A.) & BETASHE (M.). *Fasciola gigantica*, an Antigen for the Skin Reaction in Human Schistosomiasis.—*Jl. Egyptian Med. Assoc.* 1934. Dec. Vol. 17. No. 12. pp. 991-993.

Antigen from *Fasciola gigantica* tested in 130 patients passing schistosome eggs gave no intradermal reaction in 6, wheals up to 12 mm. in diameter in 20, and wheals from 13 to 25 mm. or more in diameter, mainly with pseudopods, in 104.

The antigen needs careful preparation. Fresh worms are thoroughly washed, quickly dried with filter paper, spread on glass, and dried in a vacuum desiccator. Two grams of the dried and powdered worms and 100 cc. of petroleum ether (B.P. 30-50 c.) in a stoppered flask are kept in an ice-box for 24 hours with occasional shaking. After filtering, the dry powder is extracted with dry ether for 12 hours in a Soxhlet apparatus. After removal of the ether, the powder is dried in an incubator and 0.5 gm. is emulsified in a mortar with 100 cc. of a phosphate buffer solution of pH 7.4, containing 0.5 per cent. NaCl and 0.4 per cent. carbolic acid. The emulsion is put in a shaking machine in "slow motion" for 30 minutes, left in the ice-box with occasional shaking for 4 hours, centrifuged for 10 minutes "at a high speed" which makes easier the subsequent passage of the fluid portion through a Seitz filter. The filtrate is stored in the ice-box after testing its sterility. The amount injected is 0.02 cc. Large quantities of the extract can be made at a time. C. L.

LIÈVRE (H.). Données expérimentales sur les agents thérapeutiques de la distomatose à *Fasciola hepatica*. [Experiments on Remedies for *F. hepatica* Infestation.]—*Ann. Parasit. Humaine et Comparée.* 1934. Nov. 1. Vol. 12. No. 6. pp. 511-520. [21 refs.]

The dye, Magdala rose, injected intravenously in a 1 per cent. solution is excreted rapidly, and apparently exclusively, in the bile, and has proved in the author's hands an excellent fasciocide. C. L.

- i. UYENO (Hiroshi). Ueber pathologisch-histologische Veränderungen der Kanincheniere bei experimenteller Clonorchiasis sinensis. [Histological Changes and Uric Acid Decomposition in Rabbit Kidney in *C. sinensis* Infection.]—*Okayama-Igakkai-Zasshi*. (Mitt. d. Med. Gesellsch. z. Okayama). 1934. Apr. Vol. 46. No. 4. [In Japanese pp. 794–801. [14 refs.] German summary p. 793.]
- ii. —. Ueber den urikolytischen Vorgang in der Kanincheniere bei experimenteller Clonorchiasis sinensis.—*Ibid.* June. No. 6. [In Japanese pp. 1225–1230. [23 refs.] German summary p. 1224.]
 - i. The changes dealt with are those in the kidneys, namely, cloudy swelling in acute cases and granular degeneration in chronic; they are most marked in the convoluted tubes and are caused partly by parasitic poisons and partly are the result of lesions in the liver.
 - ii. In clonorchis-infected rabbits the splitting up of uric acid by the kidney is greatly lessened as compared with the condition in the uninfected. C. L.

VÖGEL (Hans.). Der Entwicklungszyklus von *Opisthorchis felineus* (Riv.) nebst Bemerkungen ueber die Systematik und Epidemiologie. [Developmental Cycle of *O. felineus*. Classification: Epidemiology.]—*Zoologica*. Heft 86. Bd. 33. Lieferung 2/3. pp. 1–103. With 45 text figs. & 8 plates (1 coloured).

This beautiful monograph deals with investigations and experiments on the morphology and biology of *Opisthorchis felineus* from egg to adult, with certain systematic questions, and with the distribution and epidemiology of the infection.

Briefly the only snail found in East Prussia to act as first intermediate host was *Bithynia leachi* Shepp. Even *B. tentaculata* failed to do so. The miracidium fully formed in the egg as passed is hatched by the osmotic pressure of the juices in the snail's alimentary canal, and not by water; indeed when freed from the shell it is killed by water in a few minutes. The sporocyst develops close to the end of the intestine and reaches in 1 month a length of 1.2 to 1.85 mm. and the rediae then begin to leave it. Immature cercariae leave the rediae and reach maturity in about 2 months from the date of infection. They leave the snail during daylight, mostly between noon and 4 p.m., are tobacco-pipe shaped with a membrane on the tail, have a positive phototaxy and geotaxy, and are activated by agitation and a change in the amount of light falling on them.

The second intermediate hosts are the fish *Tinca tinca* and *Idus melanotus*, bottom feeders. When in contact with them the cercariae penetrate within 15 minutes and within 24 hours have begun to encyst either in the muscles of the body or the connective tissue of the head. These metacercariae grow to 3 or 4 times the original size and at a temperature of 18° to 20°C. are ripe and capable of infecting the definitive host. When the fish is eaten by this, the cysts pass the stomach unaffected, but are freed within 20 to 90 seconds of coming into contact with the juice from a fistula of the small intestine. Bile attracts the young flukes, and they travel up the bile duct into the liver within 5 hours of being swallowed. Maturity is reached, as a minimum, 4 to 4½ months after the egg left the last definitive host. C. L.

ERHARDT (Albert). Die Verbreitung von *Opisthorchis felineus* (Riv.) und anderen Katzenhelminthen in Ostpreussen. [**Distribution of *O. felineus* in E. Prussia.**—*Ztschr. f. Parasitenk.* 1934. Sept. 18. Vol. 7. No. 1. pp. 121–124. With 1 fig.]

On the eastern shore of the Kurisches Haff in East Prussia 87·8 per cent. of the cats harbour *O. felineus*. Most have more than 100 worms and some about 1,000. C. L.

EICHHOLTZ (F.) & ERHARDT (A.). Wirkungsbedingungen des Fouadins bei der Opisthorchiasis der Katze (Kombinationen mit Emetin, Wismut und Quecksilber). [**Conditions of Action of Fouadin in Opisthorchiasis of Cats.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Dec. Vol. 38. No. 12. pp. 524–534. [20 refs.]

The results of experiments on cats infected with opisthorchis, and treated with fouadin alone and in combination were not particularly satisfactory.

Fouadin in dosage of 0·1 cc. per kilo. was given to 24 naturally infected cats. In 14 of them 80 to 100 per cent. of the trematodes were killed, the others became fouadin-fast; in those in which deworming was not effected, egg laying was inhibited for 2 to 3 weeks. Emetine had but slight effect. When these two drugs were combined the latter annulled the action of the former. Bismuth and mercury were ineffective. The action of fouadin is impaired by a bad general state, by degeneration in the liver, and by other remedies given with it.

C. L.

WATANABE (Masumi). Beiträge zur Kenntnis des *Paragonimus westermanni*. (I. Mitteilung.) Ueber die *Paragonimus*-cyste in *Eriocheir japonicus*. [**Paragonimus Cysts in *Eriocheir japonicus*.**—*Okayama Igakkai Zasshi (Mitt. d. Med. Gesellsch. z. Okayama).* 1934. July. Vol. 46. No. 7. pp. 1514–1532. With 24 figs. on 1 plate. [20 refs.] [In Japanese. German summary pp. 1514–1515.]

Watanabe's investigations on paragonimus cysts in their second intermediate hosts lead him to these conclusions.

In the Okayama Prefecture, as YOSHIDA is stated to have shown already, these cysts are found in 50 to 92 per cent. of *Eriocheir japonicus* and 2 to 7 per cent. of *Potamon dehaani*. Immature cysts have a single transparent cyst wall which is digested in artificial gastric juice, yet one in nine can infect dogs; mature cysts are double walled and contain a shrunken, fully developed larva; yet the walls of cysts of all ages may be so brown as to hide the embryo. Cysts are found in the muscles and in the epithelium and blood vessels of the gut, or in the gut itself; and it is by the blood vessels that they mainly reach this viscus. They never leave the crab but at temperatures of 16° to 23°C. may live, in its dead body, in quietly running water for six weeks and for 10 to 30 days after being freed from this. [If the descriptions of the figures had been accompanied by a translation in a European language, their value would have been increased.] C. L.

BERCOVITZ (Z.) & ROGERS (J. M.). *Paragonimus westermani*. Report of Case presenting Abdominal Involvement.—*Puerto Rico Jl. Public Health & Trop. Med.* 1934. June. Vol. 9. No. 4. pp. 492–496. With 1 plate. [Spanish version pp. 497–501.]

From Southern Korea is reported the case of a woman of 29 who had *P. westermani* ova in sputum and abdomen.

Haemoptysis began in 1922; ovarian cysts removed in 1926 and 1929; abdomen contained 16 litres of bloody fluid, and when opened the peritoneum was studded with blebs or excrescences. In certain mesenteric lymph glands the ova were found in groups in the marginal sinuses, others being free of them. No worms were found in any part of the removed tissue.

C. L.

TARASSOW (Wiktor). Beiträge zum Problem des Kampfes gegen *Diphyllobothrium latum* in Nord-Westgebiet. 2. Mitteilung. [Campaign against *D. latum* in North-West Russia.]—*Arch. f. Schiffs- u. Trop.-Hyg* 1934. Nov. Vol. 38. No. 11. pp. 477–486. With 1 fig. [23 refs.]

A continuation of the description of the campaign (see PETRUSCHEWSKY & Tarassow, this *Bulletin*, Vol. 30, p. 680) shows the high percentage of broadworm infection in Karelia and about Leningrad.

The district about Leningrad with its many stretches of water is particularly heavily infected—reaching as much as 80 per cent. of inhabitants of certain parts. In 1,560 persons tabulated, the average percentage of infection was 37.1. After a treatment campaign the village percentages lay between 7.4 and 10.98. Of 405 individual strobiles the average length was between 8 and 9 metres, but in a case harbouring 143 parasites the total length of all was only 117 metres.

C. L.

PALAIS (M.). Résistance des rats à l'infestation d'*Hymenolepis diminuta* (Rud.). [Resistance of Rats to Re-infestation by *H. diminuta*.]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 36. pp. 1015–1017.

The experiments lead to the conclusion that rats infected with *H. diminuta* are resistant to an added infection.

Tenebrio molitor bred in the laboratory were infected by being fed on ripe segments of *H. diminuta*. Some were then fed to 3 rats born and bred in the laboratory. A month later they were passing onchospheres. To them and to two others were fed more *T. molitor* which, as dissection showed, were still infective. Six days later all 5 were killed. The two which had one infected feed contained 34 and 112 young *H. diminuta* measuring 6 to 35 mm. in good extension, all immature. The three who had two infective feeds contained 4, 6 and 9 strobiles measuring in good extension 130 to 660 mm. (average 240 mm.) the posterior rings being mature and ova being present in the faeces; there were no worms corresponding to the second infective feed. Protection from added infection had been produced by as few as 4 worms.

C. L.

- i. NARIHARA (N.). **Form and Colour of the Egg and Mode of its Release from the Gravid Proglottids of the Rat Tapeworm, *Hymenolepis diminuta* (Rudolphi).**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. Nov. Vol. 33. No. 11 (356). [In Japanese pp. 1611–1622. With 2 figs. [33 refs.] English summary pp. 147–148.]
- ii. —. **On the Resistance of the Egg of *Hymenolepis diminuta*.**—*Ibid.* [In Japanese pp. 1636–1646. [31 refs.] English summary pp. 148–149.]

i. The "egg's" dimensions are given to six places of decimals.

ii. Dried "eggs" on glass at 20.3° to 23.5° lived for 7 days, freed eggs in water at the same temperature for 25 and eggs in segments for 29 days, eggs in normal saline lived for a month and in 10 per cent. salt solution for 20 days. Immersion in the following solutions allowed survival in minutes for the intervals noted, the solution being of 10 per cent. unless otherwise noted: caustic potash 10, hydrochloric acid 45, sulphuric acid 15, 1 per cent. corrosive sublimate for 50 minutes in the case of some eggs, 90 per cent. alcohol 1 hour, kresol 1 hour, lysol a few eggs for 40 minutes, formalin 3 hours, urine 1 month if not changed. A moment's immersion in water at 60°C. killed them. C. L.

- NORONHA (A. J.). **A Case of *Hymenolepis nana* Infection.**—*Jl. Trop. Med. & Hyg.* 1934. Nov. 1. Vol. 37. No. 21. pp. 325–326. With 3 figs.

This case of *H. nana* infection was discovered when the stool was examined to determine the sort of dysentery from which the patient suffered. Onchospheres of the worm were found and after an anthelmintic some 50 worms were collected, 2 having heads. Thereafter the man's dysentery ceased. This is the first case disclosed in the Pathological Laboratory of the B. J. Medical School, Poona, during the author's experience of 13 years, and is believed to be perhaps the first to be reported from Poona. [CHANDLER (this *Bulletin*, Vol. 24, p. 1003) lists the incidence of this infection in 84 cases examined in Poona as 2.4 per cent.] C. L.

- BARNETT (Louis). **The Incidence of Hydatid Disease in New Zealand.**—*New Zealand Med. Jl.* 1934. Aug. Vol. 33. No. 176. pp. 191–196

Hydatid disease is increasing in New Zealand.

"From the collective statistics that I have gathered together and set forth in this paper, the following conclusions can be drawn. They give food for reflection and clearly call for a more intensive prophylaxis against hydatid infection.

"1. That hydatid disease is increasing somewhat in New Zealand. Including cases seen in private practice, a reasonable estimate is that from 100 to 150 cases are occurring every year, with a mortality of about 15 per cent.

"2. That hydatid infection is far more common in the Canterbury district than anywhere else in New Zealand. The Otago district formerly held this unenviable distinction, and now comes second on the list.

"3. That an increasing number of cases are being treated in the smaller hospitals of the Dominion."

C. L.

RILEY (William A.). **Reservoirs of Echinococcus in Minnesota.**—Reprinted from *Minnesota Med.* 1933. Dec. Vol. 16. p. 744.

Hydatid cysts have been found in 6 of 13 moose examined and the adult worms in 2 of 3 timber wolves.

Since about 450 cases of hydatid have been reported from man in Canada and the United States, M. C. HALL, chief of the Zoological Division of the Federal Bureau of Animal Industry, Washington, answered Riley's query by informing him that the strobiles had not been found there except in animals deliberately infected. Accordingly moose and wolves were examined with the results noted above.

C. L.

FENG (H. H.). **Cysticercus cellulosae Subconjunctivalis. Report of a Case.**—*Chinese Med. J.* 1934. Sept. Vol. 48. No. 9. pp. 863-868. With 3 figs. on 2 plates. [21 refs.]

A solitary cysticercus under the conjunctiva near the inner canthus of the right eye.

The cyst measured $6 \times 4 \times 2$ mm. and had been noticed for a week. There was an eosinophilia of 11 per cent. It is the first case of ocular cysticercosis found in 33,000 eye patients at the Peiping Union Medical College during the last 12 years. That it was so, was established by sections which showed a rostellum with large and small hooklets, and suckers. No dense white granule showed through the cyst wall. There were no other evident cysts nor symptoms suggesting them.

C. L.

MILLER (Harry M.), Jr. & GARDINER (Margaret L.). **Further Studies on Passive Immunity to a Metazoan Parasite, Cysticercus fasciolaris.**—*Amer. J. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 424-431.

In the transmission of passive immunity to *C. fasciolaris* the following 3 points have been established from results unpublished, previously published, and here published.

"The rat can be immunized actively against infection with the oncospheres of *Taenia taeniaeformis* and can be protected against infection by passive transfer of serum from immune animals. It has further been demonstrated that immune serum can inhibit early infections if administered within ten days."

C. L.

DE WAELE (A.). Etude de la fonction biliaire dans le phénomène de l'évagination chez les cysticerques des cestodes. [**Function of Bile in Evagination of Cysticercus.**]—*Ann. Parasit. Humaine et Comparée.* 1934. Nov. 1. Vol. 12. No. 6. pp. 492-510. With 1 fig.

The bile salts and, secondarily, choline, produce rapid evagination of the scolex of *Cysticercus pisiformis* the larva of *Taenia serrata*, and active movements of suckers and rostellum, and so presumably favour attachment to the intestinal mucosa.

C. L.

FREUND (L.). Helminthenwanderungen. III. Teil: Die Wanderungen der Cestoden von Wirt zu Wirt und im Wirtskörper. [**The Wanderings of Cestodes.**—*Ztschr. f. Parasitenk.* 1934. July 21. Vol. 6. No. 5. pp. 592-602. With 1 fig. [19 refs.]]

In continuation of previous papers [this *Bulletin*, Vol. 31, p. 373] the wanderings of cestodes in the hosts are considered. C. L.

WALANDOUW (E. K.). Nematoden als bestrijders van anopheles larven. [**Nematodes as Enemies of Anopheles Larvae.**—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Sept. 11. Vol. 74. No. 19. pp. 1219-1224. With 3 figs. on 2 plates. English summary (9 lines).]

"Description of a nematode parasitic in the larvae of a variety of *Anopheles leucosphyrus*.

"The worm is found freely moving as larva or adult outside the intestine in the body cavity of the anopheles larva. After some time the adult worm bores through the wall of the thorax or the abdomen. After the worm has come out, the anopheles-larva dies. The worm now eats the dead larva. The colour of the worm is milky white; the length is 17-20 millimeter, the width 0.052-0.088 mm.; the mouth has a spear, no teeth; the back-part ends in a tail of 0.044-0.088 millimeter."

A fuller description of the worm will be published.

C. L.

LEE (Yin). Ueber Askarideninfektion und ihre Bekämpfung. [**Ascariasis in China and its Prevention.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Sept. Vol. 38. No. 9. pp. 390-394. [10 refs.]]

The paper deals with the examination of 3,118 stools in Shanghai of which one-third showed ascaris eggs. The ascaris-infected are dealt with.

The largest number of worms recovered was 54. There are dealt with symptoms, and diagnosis from stool examination which will disclose females. Under treatment are considered santonin, chenopodium with an immediate aperient, helminal, chrysemine, hexylresorcinol and rotylon. The last has been used in 50 cases but the anthelmintic results are not clear; 10 cases certainly needed retreatment. Prophylaxis concerns itself solely with swallowed eggs, associated in China with the use of human faeces as manure. Ascariasis should be combated by treatment of school children and by the proper cooking of vegetables. C. L.

LOSSEV (L.). [**The Dehelminthization of the Surrounding Medium in Ascariidosis.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 2. [In Russian pp. 185-191.]]

The effects of high temperatures on the eggs of equine and canine ascarids are much as in the human form. Exposure to 50°C. up to one hour had no effect upon the unsegmented eggs of *Parascaris equorum*, while at 40°C. the majority were killed after 3 hours. Temperatures from 60 to 100°C. destroyed the eggs in one minute. Eggs of *P. equorum* and *Toxocara canis* containing motile embryos proved to be more resistant to high temperatures: exposure to 60°C. up to 3 minutes did not destroy the larvae immediately, but caused injuries leading to their death after several days.

Various solutions of sulphuric acid, iodine, corrosive sublimate, potassium permanganate and slaked lime failed to destroy the eggs of the ascarids, but 4 per cent. carbolic acid and quicklime killed them immediately.

C. A. Hoare.

GIRGES (Rameses). **Pathology and Complications of Ascariasis.**—*Jl. Trop. Med. & Hyg.* 1934. Oct. 1. Vol. 37. No. 19. pp. 296–300.

The pathology concerns itself with catarrh of stomach and intestine and with peri-intestinal inflammation. The complications are intestinal obstruction, intussusception, volvulus and sinus, abdominal tumours, appendicitis and its stimulation, diverticulitis, perforation, peritonitis, abscess, pancreatitis, biliary accidents, liver abscess and certain rare conditions.

C. L.

GIRGES (Rameses). **Pathogenesis of Ascariasis.**—*Jl. Trop. Med. & Hyg.* 1934. Nov. 15. Vol. 37. No. 22. pp. 340–343.

Girges deals with the hatching and transmigrations of ascaris larvae and the lesions they cause. The last reference quoted is in 1930. His indebtedness to this *Bulletin* is acknowledged.

C. L.

TSUJI (Haruo). Wirkung des Torilols, eines wirksamen Bestandteils der Früchte von *Torilis anthriscus*, Gmel., einem japanischen Volksmittel gegen Askariden. [**Action of Torilol from the Fruit of *Torilis anthriscus*, a Popular Remedy in Japan against Ascarids.**]—*Tohoku Jl. Experim. Med.* 1934. Sept. 28. Vol. 24. Nos. 1 & 2. pp. 174–194. With 3 figs.

An investigation of a fruit which is in domestic use in Japan against ascaris.

The active helminthological principle is torilol, a yellowish brown, transparent, viscid fluid with a somewhat aromatic smell and bitter taste, readily soluble in water. In earthworms, leeches and ascaris larvae it first irritates and then paralyses movements, and in the last a 1 per cent. solution produces complete paralysis in 3 hours. The minimum lethal dose by mouth per kilo. is for frogs 8 gm. and for mice 30 gm. In rabbits 1 gm. per kilo. produces no obvious change. Its clinical possibilities require investigation.

C. L.

FAZ TABO (Humberto). Nota clinica a proposito de un caso de ascaridiosis aberrante. [**A Case of Aberrant Ascaris.**]—*Vida Nueva.* 1934. July. Vol. 8. No. 1. pp. 25–29.

The patient was a boy of 4½ years of age who had complained for several days of pain in the abdomen (epigastric region), with loss of appetite and much meteorism. Having had an attack of vomiting and a marked exacerbation of the pain he was brought to hospital and while being examined there the umbilicus was observed to be prominent and a worm made its appearance through the cicatrix and its extrusion was assisted by traction. Five minutes later a second appeared and a quarter of an hour afterwards a third. All were female ascarides. There must have been a perforation of the bowel and a local peritonitis with adhesions to the abdominal wall and a fistula through which the worms passed. No operation was undertaken and recovery was uneventful, healing taking place in a few days.

H. H. S.

KELLER (A. E.). **A Comparison of the Efficiency of the Stoll Egg-Counting Technique with the Simple Smear Method in the Diagnosis of Hookworm.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 307-316.

"These data show that the dilution egg-counting technique is more accurate than the smear method for this series of examinations."

The Stoll-Hausheer method was used, that is 1/200 gram of faeces under a cover slip 25 mm. square. The smear was apparently a squash preparation of stirred faeces, an amount being used which allowed "small print" to be read when it was spread under a cover of the same size. Of 2,412 specimens examined by each method, the positive percentage results were: at the first examination 42.2 for dilution and 35.1 for smear, and after the second 44.0 and 39.4 respectively. Of specimens positive to either method 93.6 per cent. were displayed by dilution and 83.9 per cent. by the smear. The accuracy of these smears increased with the faecal egg content. By this series "the lowest level of intensity of infestation at which, for practical purposes, the smear will be of value in diagnosing hookworm infestation would be 1,200 eggs per gram of faeces instead of 600 eggs per gram as indicated by Herrick and Hausheer." It was naturally found that the number of eggs counted per smear was as feasible a method of measuring the intensity of infection as was that disclosed by dilution. These figures are also displayed as presumed worm loads. C. L.

KENDRICK (J. F.). **The Length of Life and the Rate of Loss of the Hookworms, *Ancylostoma duodenale* and *Necator americanus*.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 363-379. With 9 charts.

A model of forethought, execution and control in work carried on over 7 years on the egg production and longevity of the two common hookworms of man.

As to controls, the sanitary condition of the jail, the Madras Penitentiary, in which the work was done, appeared to exclude natural infection; but to make certain 238 prisoners, who were by D.C.F. either found to be free from hookworm infection or were treated till this was so, were re-examined by this technique at first monthly and then quarterly, and in none of them were ova discovered during the continuance of the simultaneous investigation on 30 clean prisoners who volunteered for the undergoing of deliberate infection. Both sets of men lived and worked in like conditions.

Since ancylostomes and necators are both present here and their longevity had to be separately investigated, larvae, pure specifically, were obtained by expressing ova from females of the species to be used and culturing them on sterile soil or sand. The concentration of larvae in a given suspension was evidently determined and a quantity of suspension, generally containing about 200 of them, was either placed on moist sand on the skin or given in hard gelatine capsules by mouth, it being determined that these containers dissolved in tap water in less than 20 minutes. Five oral infections were attempted with necators, a dosage of 200 larvae being given 2 to 4 times. Repeated D.C.F. examinations failed to show ova in any of them although the larvae were vigorous and their fellows produced skin infections. The other 5 necator and 20 ancylostome infections were produced through the skin. Ground itch followed at once and laryngeal irritation from the

5th day, most marked between the eighth and fifteenth days and in 2 cases persisting for over a month. Baermann's apparatus recovered larvae from the sputum of all those tested (those with the worst coughs) and in one case the numbers collected and the fact that intestinal infection failed, suggested that expectoration may be a factor in limiting this. Actually the percentage of ancylostome larvae which was accounted for as adults, recovered after anthelmintics pushed to deworming as evidenced by D.C.F., varied from one seven months after infection to about 100 eleven months after this.

Of the ancylostome infections 3 were able to be followed to their natural elimination. The intervals between infection and disappearance of eggs to D.C.F. were 81, 78 and 68 (average 76) months, whereas to the Stoll-Tseng egg counting method they were shorter by about 1 to 3 years. Similarly in the one necator case followed throughout infection lasted 61 months, but had reliance to determine this been placed on the Stoll method it would have been placed as 12 months, some 4 years too short. The counts themselves show that in ancylostome cases there is a steady rise in egg output to a peak reached 15 to 18 months after infection and thereafter a rapid decline in 3 to 6 months amounting to 50 or 70 per cent. In general the necator infections followed the same course. [This investigation had of course to leave it an open question whether this delayed reaching of the apex of egg production was due to slowness of individual worms to reach full egg laying power (in which case worm-egg ratios become more illusive than ever) or to strayed larvae slowly arriving at and maturing in the gut. Moreover it is interesting to recall that in Looss's experimental infection of a man with ancylostome larvae the greatest mean number recorded was in the 29th month, just before Looss lost sight of him.] The differences in the percentages of larvae reaching adult life could not be correlated with age—nor with previous infection since this was not known. Deaths, releases and transfers over which Kendrick had no control reduced the numbers lamentably during the course of the experiment.

C. L.

FOSTER (A. O.) & LANDSBERG (J. W.). **The Nature and Cause of Hookworm Anemia.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 259–290. With 6 graphs. [26 refs.]

"We have shown that it is *unnecessary* to postulate a toxin to account for the anemia of hookworm disease in dogs. . . . The data are in full agreement with the hypothesis that the anemia of hookworm disease is of a purely hemorrhagic nature."

The investigation was on dogs deliberately infected with *A. caninum* and bled at intervals. The first appearance of eggs was determined by D.C.F., and their numbers, when these had sufficiently increased, by the Stoll-Hausheer method. Blood samples were taken by cardiac puncture. The data are confined to the circulating part of the erythron, the marrow having been examined in no case. Five dogs were bled at intervals over periods varying from 20 to 319 days; 4 of them were already lightly hookworm infected, one was uninfected; the total amount of blood removed varied from $\frac{1}{3}$ to $1\frac{1}{4}$ of the body weight. The drop in haemoglobin was greatest in the uninfected dog (67 per cent.), from which about $\frac{1}{4}$ of its body weight of blood had been removed by 23 bleedings over 62 days [perhaps an indication that already hypertrophied red marrow in the infected cases was able to

meet the immediate attack]. "By subjecting dogs to periodic bleeding it has been possible to determine the absolute blood loss necessary to produce certain degrees of severe anaemia." [Yet the average daily abstraction of blood to the extent of 0.423 and 0.645 per cent. of the body weight produced respective drops of haemoglobin of 59.7 and 48.5.]

Although the fact of blood loss caused by worms is accepted and there is quoted the work of WELLS [this *Bulletin*, Vol. 29, p. 421] which puts the daily loss of blood caused by the individual worm as 0.8 cc. and that of NISHI [this *Bulletin*, Vol. 30, p. 686] which puts it as up to 0.484 and 0.7 cc., the authors quite arbitrarily put the figure at 0.1 cc. holding that accepting the former figures the number of worms which could produce an anaemia corresponding to the effects of bleedings is "ridiculously small," and they tabulate the number of parasitizing worms according to this assumption. Even so "it is still apparent that the blood loss caused by hookworms is a factor entirely sufficient in itself to account for the anaemia of hookworm disease in dogs." Careful tabulated work confirms the general conclusion that hookworm anaemia is microcytic and hypochromic. Nevertheless, when dogs were throughout treated with iron, cobalt and copper (2.28 gm. daily of a mixture of iron citrate 100, copper sulphate 1, cobalt chloride 5) and were given 100 larvae orally when 156 days old, the anaemia they developed was not microcytic.

Two other groups of experiments are detailed which show that there is no essential difference between the anaemias of bleeding and of hookworm infection. The authors twice refer to the inverse relationship between the number of eggs passed and the haemoglobin level, and seem disposed to consider that a rise in that level induces a resistance to the worms. Others are probably more likely to believe that death among the parasites enables the hypertrophied haemopoietic portion of the erythron to get level with the lessened blood loss. The same consideration, which is so long and well established for human infection, will explain the authors' surprise at finding how nearly the blood picture of infected dogs approaches to the normal of their never-infected litter mates.

The effects of iron therapy in producing rapid and astonishing improvement in the blood picture and almost certainly in saving life in heavily infected cases are displayed, so that "it is impossible for us to reconcile these spectacular responses to iron with the postulation that the anaemia of these dogs was caused by a toxin which paralyzed the hemopoietic centres. . . . It is our opinion that the acceptance of the hypothesis that long continued bleeding may, as an end result, cause failure of the hemopoiesis and aplasia, makes it possible to visualise nearly all of the pathology and symptomatology of hookworm disease as the complex result of chronic blood loss." C. L.

DE LANGEN (C. D.). **The Origin of the Anaemia in Ankylostomiasis.**—*Meded. Dienst d Volksgezondheid in Nederl.-Indië*. 1934. Vol. 23. Nos. 2 & 3. pp. 135-157.

"Loss of blood, diet and the condition of the intestinal canal work together in bringing about this severe and remarkable anaemia. Further investigation must teach us whether there is also a toxic damaging of the bone marrow involved in addition to these factors."

. de Langen returns to this subject (this *Bulletin*, Vol. 30, pp. 686, 812) and a comparison of the paragraph quoted above with that which ends the abstract first noted will indicate that the outline (and often the words of this paper) have been used by him before.

Loss of blood from the alimentary canal, as indicated by the benzidine reaction, is shown to be greater in those who are at work than in those confined to bed. As to eosinophilia it is shown by comparison of some 500 blood examinations that the severer the anaemia the fewer the eosinophils. "An eosinophilia is always reported as forming part of the blood picture of hookworm anaemia." [In fact ASHFORD *et al* (1911 quoting 1902) showed that in the worst cases it was absent, and that it was more useful for prognosis than diagnosis.] From this and from platelet counts it is deduced that wandering larvae are largely concerned in its production. The toxin theory of the anaemia is still without any experimental confirmation; though clinically it is held to be confirmed by the peculiar orange tint, which in S. America gives the infection the name of "the yellow sickness," a hypertrophy and dilatation of the *left* ventricle, a low diastolic and often systolic pressure, weakening of the endocrine system evidenced by lack of growth, anisocytosis and poikilocytosis in grave cases, and a megaloblastic degeneration in the last stage. Under haemolysis and regeneration the examination of 2 more cases (7 in all) sets the average life of the red cell in hookworm infection as 265 days as against 209 days for the normal native. The influences of diet on haemolysis are restated, as is the question of stimuli towards new formation of blood and the significance of diet for the clinical picture of ankylostomiasis. The question of depletion of iron reserves has, then, no mention. C. L.

CRUZ (Walter Oswaldo). *Therapeutica da ankylostomose. [Treatment of Ankylostomiasis.]*—Reprinted from *O Hospital*. Rio de Janeiro. 1933. June. pp. 471-476. With 4 figs.

The essential treatment of ankylostomiasis is iron.

It is held that all modern works on tropical medicine and the writings of most specialists concern themselves only with anthelmintics in the treatment of hookworm infection, though it is in fact a disordered iron metabolism. When iron enters the stomach in whatever form, it is ionized by the gastric juice and transformed into a ferrous salt which is immediately absorbed when it reaches that part of the duodenum where the reaction is still acid. The iron is then carried to the normoblasts in the bone marrow and there stimulates their activity. An advised dose is 3 gm. daily of reduced iron, and it has produced in 20 cases uniform regenerative changes in the red cell series of the bone marrow. The marrow is red in colour and the normoblast is held to contain in ankylostomiasis as much iron as does a normal one, but yet more iron, apparently twice as much, is needed to convert it into a red corpuscle. Deaths from this infection have occurred in Cruz's experience either from toxicity of anthelmintics, or from heart failure due to transfusion of blood, or from the failure to give iron. On giving iron there occurs a latent period of 2 or 3 days before its effects begin to appear in the peripheral blood, and during that period the serious case is in grave danger. No vermifuge should be given till the haemoglobin reaches 50 or 60 per cent. A table shows 12 cases in which after 15 days of reduced iron treatment the mean haemoglobin had risen from 32 to 48

by Sahli's instrument and the red corpuscles from 1,820,000 to 3,310,000, and reproduction of photos show how considerably the oedema had been reduced in one case in that period. C. L.

CRUZ (W. O.). [In Portuguese & English.] Patogenia da anemia na ancilostomose. Portadores de parasitos. Relação entre a atividade do helminto e a deficiência de ferro na genese da doença. **Pathogenesis of Anaemia in Hookworm Disease. Parasite Carriers. Relationship between the Activity of the Helminth and Iron Deficiency in the Genesis of the Disease.**—*Mem. Inst. Oswaldo Cruz.* 1934. July. Vol. 28. No. 3. In Portuguese pp. 391–439. With 8 figs. on 2 plates. [32 refs.] In English pp. 440–486.

Although, reputedly, the sole cause of the anaemia of hookworm disease is the hookworm, it is really of little importance in effecting this condition, for the primary factor is alimentary deficiency, a diet defective in iron.

The first of the 3 sections into which the paper falls cites from the literature conclusions of various writers, first that a distinction must be drawn between sick and carriers [the reviewer's suggestion is that no such conclusion can be drawn from the evidence], and second that the difference between the two classes depends on the food they eat. This rôle which nutrition plays is further elaborated, by quotations, in the second section, iron in food being again the point of first importance, in opposition to the view that "in fact, the most modern ideas on this helminthiasis still continue to turn around the two classical doctrines—the toxic and haemorrhagic theories." The third section deals with the pathogenesis of this anaemia. It consists essentially of the records of 5 cases followed for periods varying from over 5 to over 12 months while they maintained worm loads which as measured by eggs varied from 25,000 to 40,000 per gram of faeces.

Case 1 aged 11, with the "common diet" of rice, macaroni, potatoes and milk and 3 gm. of reduced iron daily, improved over 5 months in red cells from 1·34* per cmm. to 4·82 and haemoglobin 13 to 81 per cent. Case 2 on the same diet with ammoniacal ferrous sulphate in varying dosage of 1, 0·2, 0·05 and 1 gm. improved similarly from 2·52 to 4·70 and from 20 to 74 over 9½ months. Case 3 treated as Case 2 but with 0·8 gm. of the drug improved from 1·51 to 5·15 and from 16 to 82. Case 4 treated as was Case 2 improved from 2·53 to 4·46 and from 23 to 76. Case 5 on the common diet and 0·6 gm. of ammoniacal ferrous sulphate improved from 3·40 to 4·85 and from 30 to 88 in 5½ months and then rather more than maintained his position first with 0·3 gm. of the drug for 4 months and then with 2 underdone beefsteaks and 2 eggs daily in addition to his staple diet.

"In our cases, after normalization of blood, the most varying examinations were made, giving results approaching normal or even normal. In these patients the pathogenic action of ankylostoma and the subjective ill-feeling had entirely disappeared; the patients presented the best disposition to work and, in case of children, to play, just as occurs in infestations by inoffensive intestinal macroparasites.

"In this way we succeeded in producing experimentally carriers of ankylostoma, and thus in elucidating the preponderant rôle of food in the genesis of anaemia."

"We did not try to modify, with diet rich in iron, the blood image in initial ankylostomiasis. The negative result of such an experiment is

*Millions throughout.

clearly understood, as the iron quantity contained in these diets is, by no means, able to exert its influence upon blood. In our opinion, in ankylostomiasis the organism is in a state of martial deficiency, *i.e.*, of very diminished or even exhausted iron reserves. The quantity of these reserves is of a proportional value incomparably greater than the iron contained in food: hence the necessity of massive iron administration and not of milligrams contained even in the richest diets. The contrary is observed after the recovery of the reserve; then, the necessary doses of iron progressively diminish and even a diet rich in iron prevents the disparity of the metabolic equilibrium." C. L.

- i. RHOADS (C. P.), CASTLE (W. B.), PAYNE (G. C.) & LAWSON (H. A.). **Hookworm Anemia: Etiology and Treatment with Especial Reference to Iron.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 291–306. With 5 figs. [39 refs.]
- ii. —, —, — & —. **Observations on the Etiology and Treatment of Anemia associated with Hookworm Infection in Puerto Rico.**—*Medicine.* 1934. Sept. Vol. 13. No. 3. pp. 317–375. With 6 figs. [65 refs.]

i. Blood loss, dietary deficiency and gastrointestinal changes are apparently the causes of hookworm anaemia, and iron produces rapid improvement whether worms have been removed or not.

ii. It is held to be of practical importance that treatment should be directed first against the anaemia of hookworm disease and only secondarily against the parasites, that treatment should be by iron in large doses, and that such treatment will also be advantageous in the economical prevention of the anaemia.

The work on which both papers are based was done in 1931 under the auspices of the Rockefeller Foundation on 83 cases in hospital selected for severity of anaemia, the absence of complicating infections or source of blood loss, and the presence of hookworm ova as assured by "direct examination of the stools," which presumably means by faecal smear. The average haemoglobin by a single Sahli instrument was 32, maximum 59, minimum 8; the average red cells 2,820,000, maximum 4,580,000, minimum 780,000. In some of the cases egg counts were made by the Stoll-Hausheer method, in some worm counts by Dr. Florence King PAYNE from stools obtained after "efficient anthelmintics." Presumably the drug was hexylresorcinol since it alone, used by LAMSON'S method, is mentioned. [The reference is to the paper in this *Bulletin*, Vol. 29, p. 56, and as there noted this method left nearly half the patients still infected. There is no mention of any faecal examination after treatment; if this was undertaken by the technique mentioned it could not distinguish dewormed from infected, so that the haematological comparisons of persons before and after treatment cannot be taken as comparisons of the blood state while they were infected and after they had been freed of worms. Indeed, in a field campaign by NUÑEZ, which it is noted will be reported by her in full, three or more treatments by carbon tetrachloride and oil of chenopodium in unstated doses left a few of 32 patients with a few ova still constantly present. There was not then control of single helminthological factors.]

Biopsies of the sternal marrow were made in 15 patients and will be discussed in a later publication; the tissue was more cellular than normal, the predominant cell was the normoblast, there were islands of young cells held to be not far removed from the haemopoietic vascular

endothelium and a few held to be of the pluripotential type. The erythroblastic cells were 3 to 5 times as numerous as those of the granulocyte series, instead of both being present in about equal numbers.

As to the blood, "with the exception of the mean corpuscular volume determinations of these patients," who showed an average of 65 compared with Wintrobe's normal of 87, "nothing new is added to the blood picture of the hypochromic anaemia of hookworm disease . . . usually microcytic without evidence of active blood regeneration." The well-known fact is confirmed that there is no relationship between the degree of anaemia and the weight of infection. As regards the possibility that a toxin produced by the worms causes the anaemia, it is pointed out that the removal of the parasites should in that case increase blood regeneration, and that their presence should at least interfere with the action of blood-forming agents. In twelve cases treated with hexyl-resorcinol the subsequent general gain in red cells was trifling, in two of them these actually were reduced in numbers, and in two others the haemoglobin decreased; in fact the same state of affairs showed itself as in cases watched without removal of worms.

In the absence of evidence for deworming it cannot be admitted that the authors have worked under the conditions necessary for proving their first point; but their work does show strikingly first that improvement of diet obtained by adding to the normal food of these islanders 300 gm. of meat and 1,500 cc. milk did not improve the anaemia of 8 very anaemic and still infected patients who were given no anthelmintic; and second that the administration of 6 gm. of iron and ammonium citrate did so with reticulocytosis, so that the haemoglobin was raised during the varying periods of observation to between 47 (after 18 days) and 70 per cent. (28 days). In a case in which the gastric juice contained no acid on stimulation by alcohol or histamine there occurred within 18 days of beginning iron a rise of red cells from 1,500 000 to 3,400,000 and of haemoglobin from 20 to 40.

A chart illustrates the striking difference between the good effect of removal of parasites in malaria [in which iron from the destroyed parasites is stored in the body] and the negligible effect of so treating hookworm infection [in which it is passed into the lumen of the gut]. Under the heading "The effects of blood loss" it is remarked that injection of washed red cells seems to have a haemopoietic effect as evidenced by a gain of nearly two million red cells and 9 per cent. haemoglobin in one case and a reticulocytosis of 12.6 per cent. in the other, the worms being left in both. As to dietary, it is concluded that the basal diet of these persons contains in peas and beans a reasonably good source of iron, and failure to use it is attributed to lessening of assimilative power.

As to treatment, it is said that ASHFORD, KING and IGARAVIDEZ held in their well known report on *Uncinariasis in Porto Rico* that "elimination of hookworms would bring about rapid relief of anaemia in the majority of cases" and that they "did not consider therapy with iron of any particular importance." These writers actually wrote as follows:—"The object of treatment is of course to remove the cause by expulsion of the worms. In many light and moderate cases this will suffice, but in old and chronic cases, and those where the disease has reached a severe grade, some regenerative treatment should follow the specific," and again, referring to tabulated results, "It will be noted that slight cases readily recover without iron." The present

authors were, as stated, deliberately dealing with severe or very severe cases. Gastric anacidity was present in 24 per cent. of 54 cases, but, apparently irrespective of this, the effects of iron and ammonium citrate in daily doses of 6 gm. were good. This drug produced as a rule, but not always, a considerable improvement in the blood even when the worms were left. Of the liver preparations, satisfaction was obtained from an aqueous extract only. Improved diet was without notable effect.

This preparation of iron is suggested as a cheap preventive of the anaemia either with or without an anthelmintic. "It is to be hoped that since the symptomatology of hookworm infection is predominantly that of anaemia, the primary importance and simplicity of dealing directly with the anaemia will be appreciated by those engaged in the problem." [That is to say, when considering prophylaxis the hygienist should primarily treat a symptom and relegate to a subordinate place the getting rid of the grave source of infection for others, which in rural tropical districts is constituted by the faeces of the hookworm infected.] C. L.

SFAMENI (Mario). Ricerche sulla diffusione dell'anchilostomiasi in limitate zone della provincia di Messina. [**Ankylostomiasis in a District of the Province of Messina.**—*Riforma Med.* 1934. Oct. 27. Vol. 50. No. 43. pp. 1650-1652.]

In a part of the Province of Messina, comprising Scala, Casino, S. Biaggio and Pirrera, the author, who is Health Officer of Torregrotta (Messina), found a considerable number of persons infested with hookworm, some presenting no symptoms of disease. In Scala he found ova in the faeces of 77 out of 292 persons examined; in Casino the same number in 201 examined; all were of the peasant class. [The technique used is not mentioned.] H. H. S.

SCHWARTZ (Benjamin) & ALICATA (Joseph E.). **Development of the Human Hookworm, *Necator americanus*, in Guinea Pigs.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 317-328. With 2 figs.

N. americanus followed in the guineapig its normal development up to the 16th day.

Infection took place both by mouth and skin, and in both cases larvae took the pulmonary circuit. In the lungs they produced the usual haemorrhages and showed signs of an approaching moult. After the 9th day all had left the lungs for the intestine in which they were not found at 24 days, though at 16 they showed the provisional mouth capsule with beginning sex differentiation. C. L.

FOSTER (A. O.) & CROSS (S. X.). **The Direct Development of Hookworms after Oral Infection.**—*Amer. Jl. Trop. Med.* 1934. Nov. Vol. 14. No. 6. pp. 565-573. [22 refs.]

For intra-corporeal development of the larvae of *Ancylostoma caninum* the lung journey is unnecessary, and when they are given orally to the optimum host they usually develop directly in the intestine without a pulmonary migration.

Of 8 dogs two were kept as controls; in the others 6 oesophageal fistulae were made, the upper end of the oesophagus being brought out

on one side of the neck the lower end on the other, the latter being firmly bandaged with a pad saturated with a concentrated suspension of santonin and calomel which it was felt would act as a larvicide. Three of the fistulated dogs were infected orally* (2, 5 and 0 days after the operation) as was one control. The other 3 fistulated dogs were infected by skin (1, 0 and 0 days after the operation) as was the other control. As to the orally infected, from the control 39.84 per cent. of the larvae were recovered as worms from the intestine when it died on the 10th day, and from the others 37.02 per cent. when killed on the 26th day and 47.43 after death on the ninth day, while from the third which died on the 3rd day 330 of 2,800 larvae were recovered from the intestine and none from the lungs. As to the skin infected, 7.65 per cent. of the larvae applied were accounted for as worms in the control dog, and in the others 0.14 per cent. and 0 per cent. in dogs killed on the 26th and 15th days; and in one which died on the third day 224 of 2,800 larvae were found in the lungs and none in the intestine.

These results show that the lung journey is not necessary for development to maturity of *A. caninum*, they "give added support to the earlier work of LOOSS and FÜLLEBORN which indicated that the normal path of migration of nematode larvae was by way of the trachea and oesophagus" and they suggest that the heavier infections which occurred after oral administration may be partly attributable to an escape by the larvae of such hazards as are associated with migration. It is held that the extensive studies which have been made by observers show that orally administered larvae of *A. caninum* and perhaps of *Uncinaria stenocephala* migrate from the alimentary canal in non-optimum but not in optimum hosts, so that in the case of other nematodes one cannot without direct evidence assume a pulmonary journey.

C. L.

YOKOGAWA (S.). **Experimental Studies on the Question why the Mature Larvae of Ancylostoma when ingested by an Improper Host migrate in the Body, and do not migrate when given to the Proper Host.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1934. Sept. Vol. 33. No. 9 (354). [In Japanese pp. 1254–1258. With 4 figs. on 1 plate. English summary pp. 122–125.]

The conclusions appear to be based on blood agar plates and on experiments on 5 animals, using infective larvae of *Ancylostoma caninum*.

"From these experiments with rabbits and dogs we learn that the penetration of mature larvae of *Ancylostoma* into the wall of the stomach is influenced very much by the physical conditions inside the latter; however, this penetration is not controlled exclusively by physical conditions, but seems to depend much more on the biological nature of the host, because in an improper host, the rabbit, in spite of the presence of water in the stomach, a majority of the larvae entered the wall of the stomach, while on the other hand in their proper host, the dog, the larvae found it difficult to penetrate into the wall of the stomach even under modified conditions that must be expected to stimulate their thigmotropism toward the wall of the stomach."

C. L.

* The terms used consistently in the paper are "orally" or "*per os*." Presumably infection was produced in the same way as feeding was effected, namely by stomach tube passed down the distal oesophageal opening.

TIMPANO (P.). La velocità di sedimentazione dei globuli rossi, la resistenza globulare e il tempo di coagulazione del sangue degli anchilostomiasici. [*Velocity of Red-Cell Sedimentation, Red-Cell Resistance and Coagulation Time in Ankylostome Infection.*]—*Ann. d'Igiene.* 1934. Sept. Vol. 44. No. 9. pp. 806-812. [19 refs.]

The cases examined number 30, the controls 5, but the paper does not state the diagnostic method used so that the freedom from infection of the controls is a matter of conjecture.

The finding is that the velocity of sedimentation is increased, the resistance of the red cells lessened and the time of coagulation lessened as compared with anaemics which are held to be uninfected. The changes do not suffice for diagnosis; their implications on prognosis it is proposed to investigate. C. L.

FAUST (Ernest Carroll), WFLS (Joseph W.), ADAMS (Corine) & BEACH (Ted D.). **Experimental Studies on Human and Primate Species of Strongyloides. III. The Fecundity of Strongyloides Females of the Parasitic Generation.**—*Arch. Pathology.* 1934. Nov. Vol. 18. No. 5. pp. 605-625. With 3 figs.

The paper of which that abstracted in this *Bulletin*, Vol. 31, p. 800, forms a preliminary note (as was conjectured).

The search for adult worms at autopsy was made by washing away and examining the gastric and intestinal contents and scraping off of the mucosa and submucosa of oesophagus, stomach and intestines; the adult worms were counted. Moreover, as was not gathered from the preliminary note, the trachea and bronchi were similarly treated, and the lungs chopped and strained. Great care was thus taken in the attempt to obtain all worms. It cannot always have been successful since in one of the 17 dogs 600, 800, 150 and 300 larvae were found in 5 gm. portions of faeces during the last 4 days of its life, but when killed all of the 608 female worms found were non-fecund and encapsulated. Similarly in another dog passing in like manner 3, 481, 770, 785 and 2,479 larvae, only a few eggs were found in a small proportion of the 708 female worms disclosed, most of them appearing to be post-productive. The authors' summary is as follows:—

"On the basis of an intensive experimental study of human *Strongyloides* in young dogs and of a chimpanzee strain of the organism in a rhesus monkey, concrete evidence has been obtained, indicating that following the period of incubation the parasitic female worms produce eggs, the number of which rapidly increases and then gradually decreases to zero. This phenomenon is due not to the escape of the worms from the mucosa of the upper levels of the small bowel, but to reactions in the tissues of the host, including first encapsulation of the egg-laying females and later cellular infiltration around, and phagocytosis of, the worms. Ordinary fecal examination for larvae of *Strongyloides* has been found a very unsatisfactory criterion of the presence or numbers of parasitic females, in view of the frequent disintegration of larvae en transit down the bowel and because of the gradual reduction in the egg production of the mother worms. Although fecal examinations may consistently fail to disclose the organism for a period of weeks or months, a considerable number of female worms may still be present in the duodenal and jejunal mucosa and be responsible for chronic toxic manifestations. Internal infection (hyperinfection) is offered as an explanation for prolonged human strongyloidosis."

C. L.

SPINK (Wesley W.). **Effects of Vaccines and Bacterial and Parasitic Infections on Eosinophilia in Trichinuous Animals.**—*Arch. Intern. Med.* 1934. Nov. Vol. 54. No. 5. pp. 805–817. With 5 charts. [16 refs.]

These studies were undertaken to decide the question whether in trichiniasis secondary infections may reduce the number of eosinophils to such an extent as to make the diagnosis uncertain. Guineapigs were used.

"1. The number of circulating eosinophil leukocytes in animals infected with *Trichinella spiralis* was reduced following infection with *B. tuberculosis*, *Staph. aureus* and *Trypanosoma equiperdum*. Animals which had received repeated injections of typhoid vaccine responded with a rise in the eosinophil level. No change was noted following the injection of heat-killed tubercle bacilli.

"2. Studies of the bone marrows from the same animals did not reveal a corresponding decrease in the number of eosinophil cells.

"3. Trichinous animals having a superimposed infection of tuberculosis or trypanosomiasis had less reaction around the encysted parasites in the muscle than the control animals. Trichinous animals inoculated with typhoid vaccine showed similar changes in the muscles.

"4. Trichinous animals subjected to a high level of dry heat responded with an absolute rise in the circulating eosinophilic leukocytes.

"5. No relationship was found between the weights of animals and the level of eosinophilic leukocytes in the peripheral blood.

"6. The number of circulating eosinophil cells did not appear to be related to the mode of encystment of *Trichinella spiralis* in the muscle."

C. L.

BACHMAN (G. W.), MOLINA (R. Rodríguez) & GONZALEZ (José Oliver). **Anomalous and Non-Specific Reactions with *Trichinella spiralis* Antigen in Relation to Other Disease Conditions.**—*Amer. J. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 415–423.

A titre of 1 in 2,500 and above in terms of dry weight of powder can, according to the experience of the authors, be termed specific for trichiniasis in 90 per cent. of cases.

"Of the 857 sera studied . . . the titers varied from 1 : 100 to 1 : 3,000. In the precipitation test of the various groups, 18.06 per cent. gave a titer of 1 : 100 ; 19.4 per cent., 1 : 200 ; 41.6 per cent., 1 : 500 ; 11.9 per cent., 1 : 1,000 ; 4.0 per cent., 1 : 1,500 ; 2.8 per cent., 1 : 2,000 ; 2.08 per cent., 1 : 3,000.

"We may deduce from these investigations that the precipitation test for the diagnosis of human trichiniasis does possess a fairly high specificity in relation to other disease conditions. It is the experience of the authors that the presence of the anomalous reactions can be easily differentiated from the true, positive precipitation rings. According to the results of the authors, non-specific precipitation reactions occur in low dilutions at the interphase of the serum and test-antigen, and give rings similar to a true precipitation ring in Wassermann and Kahn reactions and parasitic infestations as well as in conditions where there is nitrogen-retention and increased cholesterol and chlorides in the blood."

C. L.

BACHMAN (G. W.) & OLIVER (J.). **Virulence of *Trichinella spiralis* in a Natural and in an Experimental Host.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Oct. Vol. 32. No. 1. p. 96.

On successive passages through abnormal hosts trichinella seems to lose in virulence and infectivity.

Repeated rat to rat feedings of trichinous flesh, obtained by killing infected rats at 20-day intervals, given in sub-lethal quantities produced increased infections as measured by the number of larvae in each gram of flesh. Repeated rabbit to rabbit feedings resulted in the dying out of the infection after 5 passages. C. L.

NIÑO (Flavio L.). Consideraciones clínicas y parasitológicas acerca de una observación de triquinosis humana. [**Observations on a Case of Human Trichinosis.**].—*Semana Méd.* 1934. Aug. 16. Vol. 41. No. 33 (2118). pp. 461-488. With 47 figs., 4 plates & 1 graph. [38 refs.]

A very detailed account of a man, 63 years of age, an Italian in the Argentine, who suffered from a subacute suppurative myositis of the left infrascapular region. Operative measures revealed the condition to be due to numerous *Trichinella* cysts. The pathology is described very minutely and the text is illustrated by no less than 66 figures, mostly microphotographs. The author is of opinion that many cases are missed, being diagnosed as suffering from influenza, or rheumatic pains. In 1916, at a Hygiene and Pathology Conference, it was reported that 4 per thousand of the pigs examined in the slaughter houses of Liniers were trichinosed, and ten years later this proportion was doubled in spite of the measures of inspection and prevention. H. H. S.

EILMANN (H.). Verkalkte Trichinellen in Bärenfleisch. [**Calcified Trichina in Bear's Flesh.**].—*Deut. Tierärztl. Woch.* 1934. Vol. 42. No. 39. pp. 633-635. With 9 figs.

Although not too appropriately placed in a Bulletin catering for tropical readers it may be recorded for completeness that trichinosis is reported in a polar bear. C. L.

GRAHAM (G. L.). Resistance Studies with the Nematode, *Nippostrongylus muris*, in Laboratory Rats.—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 352-372. With 2 figs. [12 refs.]

A study of helminth "resistance."

"The development of an acquired resistance by rats against reinfection with the nematode parasite, *Nippostrongylus muris*, has been confirmed. It has been shown that the degree of acquired resistance developed is associated with the size of the initial infection, i.e., the heavier the primary worm burden the greater the resistance developed. Repeated exposure to increasingly large numbers of larvae at weekly intervals has been shown to result in the development of a marked resistance as judged by egg count. The resistance was shown to be initiated by comparatively light infections.

"The evidence from the present experiments indicated that 'physiological crowding' of a degree like that observed with *H. spumosa* in rats and *A. lineata* in chickens was not present. However, this does not preclude the possibility that a demonstration of this host-parasite phenomenon can be achieved by suitable methods." C. L.

SWEET (W. C.) & DIRCKZE (H. A.). A Filariasis Survey of the Southern Province of Ceylon.—*Ceylon Jl. Sci.* (Sect. D. Med. Sci.) 1934. Dec. 8. Vol. 3. Pt. 3. pp. 177-182. With 1 map.

The authors give the following account of their survey:—

"A rapid filariasis survey of the Southern Province of Ceylon was made between November 16, 1925, and January 15, 1926, by the staff attached to the Anchylostomiasis Campaign. During the survey night blood specimens were taken from 3,371 persons, of whom 163,

or 4.8 ± 0.3 per cent., were found to have microfilariae in their blood. Forty-two cases of elephantiasis were seen by or reported to the staff. Since eleven of the cases of elephantiasis also showed microfilariae in their blood specimens, the total filariasis rate for the Province was 5.8 ± 0.3 . The microfilaria rate of males was not significantly different from that of the females examined. . . . All the infections were patchy in distribution. The filaria concerned was assumed to be *W. bancrofti*. No study of mosquito vectors of the disease was attempted." C. L.

Hu (Stephen M. K.). **An Examination of Prisoners at Paoshan, Kiangsu Province, for Microfilariae of *Wuchereria bancrofti* Cobbold.**—*Chinese Med. J.* 1934. Nov. Vol. 48. No. 11. pp. 1143-1145.

The results of examination of thick blood films taken between 9 p.m. and midnight from 146 prisoners are set out.

Of 140 males 24 showed microfilariae and of 6 females 3 did so. Of the 27 positive cases 17 were natives of the Paoshan district and 26 of the Kiangsu province. C. L.

Voss (J. A.). Et tilfelle av filariose. [**Case of Filariasis.**]—*Norsk Mag. f. Laegevidenskaben*. 1935. Jan. Vol. 96. No. 1. pp. 17-21. With 1 fig. French summary (4 lines).

Voss describes from Norway a case of filariasis contracted in Tahiti and stresses the importance of bearing in mind tropical disease when treating patients in temperate climates. C. L.

RODENWALDT (Ernst). *Filaria malayi* im Delta des Serajoe. II. [*Filaria malayi* in the Serajoe Delta [Java].]—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië*. 1934. Vol. 23. No. 1. pp. 21-43. With 2 figs. & 6 plates.

In spite of an inadequate and somewhat misleading title, this paper is purely entomological, and is concerned with presumptive mosquito vectors, rather than with *Filaria malayi* itself.

As is now well known, *Taeniorhynchus* (*Mansonia*) larvae have the remarkable habit of obtaining oxygen from the roots of water plants, to which they attach themselves by their siphons. Four attempts, with close examination of water plants, to find *Taeniorhynchus* larvae in the Serajoe delta proved fruitless, despite the fact that species of the genus, especially *M. annulifera*, were present and attacked the local inhabitants throughout the year. Laboratory experiments in Batavia, using 234 living adult *Taeniorhynchus* (chiefly *M. annulifera*), swamp water and water plants, especially *Pistia stratiotes*—all obtained in the Serajoe delta—were more successful. The author gives a detailed and well illustrated description of the egg and first and second stage larvae of *M. annulifera*, which, like *M. indiana*, deposits its eggs in rafts attached to the under (submerged) side of the edges of *Pistia* leaves. One raft consisted of 129 eggs. The egg and young larva of *M. indiana* are also described. Laboratory conditions proved unfavourable, and no larva pupated; but the investigation is being continued.

Possible vectors of *Filaria malayi* are briefly discussed. Of mosquitoes caught on human beings, the only species found infected were: *M. annulifera* (73.6 per cent. out of 91 individuals), *M. uniformis* (8 out of 12), *M. indiana* (5 out of 7) and *Anopheles hyrcanus* (16 out of 18).

[For I of this series see this *Bulletin*, Vol. 30, p. 697.]

E. E. Austen.

RODENWALDT (Ernst). *Filaria malayi* im delta des Serajoe. III. [*F. malayi* in the Serajoe Delta.].—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië*. 1934. Vol. 23. No. 4. pp. 194–212. With 17 figs. on 7 plates.

The intermediate hosts and antigen reactions of *Filaria malayi* are considered.

The first section considers the structure of *Mansonia annulifera* and *M. indiana* in their different stages, the second the distribution of mosquitoes during a year at two spots in the Serajoe delta. The third section deals with the local manufacture of dried dirofilaria antigen, dissolved in fifty times its quantity of a mixed salt solution as used by MCCOY, MILLER and FRIEDLANDER and diluted to as much as 1 in 5,000 to 1 in 10,000. Good immediate reactions were obtained equally in 5 cases of elephantiasis without microfilariae, in 5 cases with *Mf. bancrofti* in the blood, and in two natives of the country from a locality where this infection was unknown and who were used as controls. In view of the unspecific character of the reactions which were obtained, the possible use of the adult *F. malayi* when it has been isolated is mentioned, and the difficulties involved in discovering it are pointed out.

C. L.

RAY (P. N.). **Filarial Affections of the Male Genital Tracts.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 554–558. With 8 figs. on 1 plate. [13 refs.]

The note draws attention to some recent advances in knowledge of filarial affections of the male genitalia.

These are considered under the following headings. Lymphatic varicocele should not be excised for fear of cellulitis or chylous fistula; sodium morrhuate injection produced thrombosis in one case. Endemic funiculitis is due to a secondary bacterial infection and half to three-quarters of sufferers die. Hydrocele needs mention only. Chronic epididymo-orchitis is being dealt with in connexion with a case now in the press. Under elephantiasis of scrotum and penis Ray finds confirmation of the reviewer's suggestion, that infective larvae reach the site by the blood escalator, in the consideration of the fact that this condition is very rare in children and that before puberty the blood supply to the parts is little developed. Lymph scrotum is described. In inflammatory reactions the author has failed to obtain evidence of secondary infection.

C. L.

GRACE (Arthur W.). **Filarial Lymphangitis, considered as a Mild Erysipelas resulting from Hypersensitiveness to a B. Haemolytic Streptococcus of a Particular Type.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 259–276. With 2 charts. [21 refs.]

The author now feels that the hypothesis of streptococcal latency [this *Bulletin*, Vol. 29, p. 73] is a less satisfactory explanation of recurrent filarial lymphangitis than one based on a tuberculin-like allergy of the affected tissue resulting from numerous minor infections of that tissue.

The argument runs thus. First, evidence that a bacterium is the exciting agent. Clinically the attack resembles that of the mild erysipelas of New York in which, too, a history of previous attacks is

common. Of 110 lymphangitis cases 64·5 per cent. developed abscesses and in all but one the organism was the β -haemolytic streptococcus. Subcutaneous nodules covered by red brawny skin occur in a tenth of lymphangitis cases and in a tenth of them [*i.e.*, presumably in 1 per cent. of the nodules] the same streptococcus is found in pure culture.

A case is described with two nodules, one in the left forearm which subsided, and one in the right leg which suppurated, and the author adds, "It is difficult to believe that the nodule which subsided was due to *Wuchereria bancrofti* and that that which suppurated was the result of pyogenic infection" [could not one become secondarily infected and the other not?]. The conception of O'CONNOR's "focal spots" (in which worms have been demonstrated on excision) is that the parasites have nothing to do with their causation, for the worms are so many, it is held, that when a spot is excised it is pretty sure to have one in it, and this will be dead because it has been killed by bacterial toxin. Blood counts during lymphangitic attacks are identical with those of erysipelas, a leucocytosis with polymorphonuclear increase, yet in convalescence there is often an eosinophilia. As to 40 blood cultures in 35 patients, 6 were positive in 4 patients. MCKINLEY found none positive in 24. Grace holds it apposite to note that on adding the two together the positive rate is under 7 per cent., much in keeping with the result of blood culture in erysipelas. The morbid histology as described by O'CONNOR for acute filarial lymphangitis and MACCALLUM for erysipelas is held to be suggestive of both being erysipelas, though plasma cells, large mononuclears and eosinophils are specifically mentioned in one case and not in the other.

In spite of the stress laid on the similarity of filarial lymphangitis to erysipelas of temperate climates, evidence is offered which is held suggestive that the β -haemolytic streptococcus associated with filarial lymphangitis differs from that commonly met with in temperate climates and is an organism of low virulence. Comparisons of British Guiana with Jamaica, and of the black with Chinese or European populations of Georgetown, British Guiana, leads to the conclusion that the incidence of lymphangitis and elephantiasis among communities is independent of their microfilarial rates, but is correlated with their standard of living and their use of footwear.

The conclusion that the condition is a manifestation of hypersensitiveness to this haemolytic streptococcus is based on reactions to non-haemolytic streptococci, on the fact that it is rarely associated with any organism other than the β -haemolytic streptococcus, that the age incidence of positive Dick tests favours it; so do the presence of the subcutaneous nodules already mentioned, its high incidence in the lower limbs, the low incidence of positive blood cultures, and the mildness of constitutional symptoms. In fact there is held to be no evidence that *W. bancrofti* plays any part in the production of these lymphangitic attacks.

C. L.

DE (M. N.) & CHATTERJEE (K. D.). **Streptococcal Septicaemia and Filarial Orchitis.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 558-560. With 3 figs. on 1 plate.

A discussion of 3 cases among 75 consecutive autopsies leads to the conclusion that the rôle of filarial infection in the causation of fulminant streptococcal septicaemia, though very definite, is not yet fully understood.

The organism found locally or in the blood in all was *Streptococcus haemolyticus*. If it produces little pus formation prognosis is serious. In none of the cases could any source be found for an exogenous infection. It is held as an established fact that in males filarial infection usually remains localized in the genitalia, in which place the streptococcal lesion occurs and the association is explained as possibly due to an upset symbiosis or to some condition of "soil" produced by the worms which is suitable for the streptococcus. C. L.

MENON (T. Bhaskara) & ANNAMALAI (D. R.). **Some Pathological Changes met with in Filarial Orchitis and their Significance.**—*Jl. Trop. Med. & Hyg.* 1935. Jan. 15. Vol. 38. No. 2. pp. 18-21. [13 refs.]

Examination of 5 cases leads to the conclusion that the ordinary changes in filarial orchitis are those of foreign-body reaction, and that they are quite different when a microbic infection is added.

The type of inflammatory reaction round worms shows in the tissues clusters of lymphoid cells, eosinophils and mononuclears with a few plasma cells and very few polymorphs, and with large giant cells about the periphery. These last appear to arise partly by fusion of the endothelial histocytes which border the worm node. Local endolymphangitis obliterans with dilatation and hypertrophy of the muscular coat was present. In one case three female worms, alive at operation, were present and all showed the same stage of pregnancy, extreme distension with embryos, so being, it is noted, in agreement with the reviewer's view, that parturition is simultaneously timed. In the other case the females when present were solitary [the hour of operation is not noted in any case]. In the fifth case there were large clusters of polymorphs showing the degenerate nuclei of secondary bacterial invasion. C. L.

HOMANS (John) & (by invitation) Cecil K. DRINKER & Madeleine FIELD. **Elephantiasis and the Clinical Implications of its Experimental Reproduction in Animals.**—*Ann. of Surgery.* 1934. Oct. Vol. 100. No. 4. (Part 502). pp. 812-829. (Discussion pp. 829-832). With 11 figs. [25 refs.]

The paper studies the composition and movement of tissue fluid in experimental and clinical elephantiasis, the condition of the lymphatics therein, and the clinical and surgical implications of the conditions disclosed.

There has been no success in establishing elephantiasis in animals by repeated removal of lymph glands, nor is there positive support for suggestions that the condition is due to disorder of chemistry and water balance in the tissues or to malformation or varicosity of lymphatics. A case is described where pelvic exploration showed scarring of lymphatics over the left pelvic brim, but to be successful in treating the condition operation would have to be early before the lymph vessels in the limb have been obliterated by elephantiasis. That they are so has been proved in experimental filariasis in the dog (*cf.* this *Bulletin*, Vol. 31, p. 806). Thus in the normal dog, when a suitable dye is injected between the toes, light massage causes rapid filling of the whole lymphatic tree, and the lymph vessels can, by the skilled, readily be cannulated. In the dog made elephantoid experimentally, no vessels

are visible, but the dyed lymph can, if the creature is white-skinned, be seen drifting about up or down the limb according to the animal's position, the movement being solely due to gravity. Exactly the same condition has been demonstrated in elephantiasis in man, the sclerosing process has destroyed all vessels and the dye as seen in the skin drifts about in the lymph-soaked tissues according to the position of the limb; using thorotrast and X-rays the same effect is demonstrated. Some skin areas have, however, remained uncoloured in these conditions, evidently because there the lymphatics are efficient; so that if something in the nature of an Auchincloss operation is attempted, there is no object in removing skin higher than the point at which lymph, as shown by such a test, is carried off with reasonable efficiency; and any operation designed to empty the lymphatics of the lower limb into the retroperitoneal sac cannot expect success unless performed before the lymphatic vessels have been destroyed by increasing elephantiasis. Both lymph and tissue fluid in this condition have from 2.7 to 5 per cent. of protein, instead of the normal 1 per cent., and haemolytic streptococci can be cultivated from the tissue fluid of the elephantoid dog in the early hours of each lymphangitic attack but at no other time

C. L.

FERNANDO (S. E.). **Ocular Filariasis. (Adult *Wuchereria bancrofti* in the Anterior Chamber of Human Eye).**—*Jl Trop. Med. & Hyg.* 1934. Jan. 15. Vol. 38. No. 2. pp. 17-18.

The symptoms caused by a worm in the anterior chamber of the left eye and the description of the creature itself are given.

Turbid aqueous humour obscured the fundus of the red, painful and photophobic left eye, but in the anterior chamber was visible a whitish, threadlike worm in ceaseless coiling movement. It was removed through a corneal incision with complete recovery of the eye. Its full published description is as follows:—

“ The nematode submitted for identification is *Wuchereria bancrofti*, a member of the subfamily Filarinae (order Filarioidea).

“ Its full length cannot be ascertained as the posterior region is missing. Its present length is less than 90 mm. The females of *Wuchereria bancrofti* reach a length of 100 mm., so that it is possible that the present specimen might have been a full-sized female.

“ A description of the worm in its present condition is as follows:— It is very delicate, and tapering anteriorly. There is a distinctly enlarged, rounded head followed by a neck. The head bears two rows of papillae. The mouth is terminal and is not surrounded by lips. Oesophagus is long, showing indications of division into two parts. Female genital aperture is slightly posterior to the middle of the oesophagus.’ ”

The man, a Singhalese, did not come from an endemic filarial area, nor were there microfilariae in the night blood.

C. L.

i. LOW (G. Carmichael) & MANSON-BAHR (P. H.), with a Laboratory Report by A. H. WALTERS. **Further Observations on Filarial Periodicity.**—*Lancet.* 1934. Sept. 8. pp. 531-535. With 2 figs.

ii. LANE (Clayton). **The Periodicity of *Microfilaria bancrofti*.**—*Ibid.* Dec. 29. pp. 1437-1441. [11 refs.]

i. The authors have studied another patient suffering from filariasis [see this *Bulletin*, Vol. 30, p. 703] with a view to testing the periodicity

of the appearance of embryos of *W. bancrofti* in the peripheral circulation. The subject was a lascar in whose blood at night these embryos were present in large numbers. Two series of observations were made. In the first, for 4 consecutive days 2-hourly counts were made of the embryos present in 20 cmm. of blood. On the first two days the maximum appeared in the 2 a.m. count, on the last two at midnight. This is explained by the patient falling asleep earlier on these days "thus giving an impetus to an earlier influx of embryos." The total numbers found were fairly approximate with an average of 417 in the 24 hours.

In the second experiment, counts were similarly made at first for 4 days and later for 8 days with the patient reversing his usual habits and turning day into night. [In the text the counts were said to be made 2-hourly in the former period and 4-hourly in the latter, but the graph shows a 2-hourly count throughout, in spite of the statement which occurs more than once that he slept for 4 consecutive hours.]

In the second experiment no irregularity was noticed on the first day; on the second there was a less rapid fall between midnight and 6 a.m., and a more marked irregularity on the third day. On the fourth the peak was reached at 4 a.m. and the noon figure was 26 compared with the midnight 47; this the authors describe as "a marked fall in the total number of embryos at midnight . . . counterbalanced by a marked increase of total numbers at midday." On the 5th to 8th days, the midnight numbers were 40, 59, 53, and 55, the peak being reached at 2 a.m. except on the last day when it was at 4 a.m., and the noon counts were 23, 67, 37, and 48. Only once, therefore, on the 6th day was the noon count higher than that at midnight. The average for the whole 24 hours was higher than under the normal conditions, namely, 448 for the complete period, and 463 for the last 4 days in place of 417. The minimal counts in the last period occurred from 6-8 p.m. The authors infer that it is likely that the same number of embryos are passed into the blood stream every 24 hours, regardless of the habits of the patient and that there is daily migration and reappearance of the same undamaged embryos.

A fortnight after the patient resumed his ordinary mode of living the normal nocturnal periodicity returned. They conclude that periodicity is in some manner dependent upon the habits of the human host and that "irregular periodicity" is a better term [some would regard this as a self-contradictory term]. Thirdly, that the minimum number of embryos in the circulation, whether in reversed or normal life, occurs at about 6 p.m. This is shown to be truer in the reversed than the normal graph in this article.

The authors also carried out an experiment with a guineapig the bearing of which on the argument the reviewer is unable to appreciate. They injected blood containing some 23,000 live embryos into the heart of a guineapig which was killed 5 minutes later and on examination no embryos could be found in the heart blood or organs. Clearly in this case they did not hide in an internal organ and no opportunity was given for them to reappear. It would appear to favour the argument that they were all killed off. [The authors explain this by saying that "the moment they (the embryos) are transferred to incompatible blood they perish." The fact that "none were found" is taken as "none were present." This is, perhaps, hardly justifiable as it would surely be without parallel in pathological experience. From the authors' point of view, however, this absence is, it seems, implied.]

On the *mechanism* of filarial periodicity the authors offer no fresh evidence. They describe the classic cases of MANSON, when the patient died suddenly after a dose of prussic acid and that of an infected Barbadian who died at 10 a.m. and embryos were found in the lungs only. The authors take for granted that the embryos in the first case must have been immediately immobilized "owing to the large dose of the prussic acid taken" and in the second they [so it appears to the reviewer] rather beg the question by assuming that lymph flow ceases immediately on death. Their considered opinion is thus stated in conclusion:—

"We . . . believe that filarial periodicity is best explained by parturition going on more or less continuously, the young being, as Manson put it, nearly constantly carried along the lymphatics and thoracic duct to the blood, while the excess that would in time take place is checked and kept more or less constant by a mortality amongst the older and effete embryos."

[This would equally well, perhaps better, account for absence of periodicity.]

ii. Col. Clayton Lane begins by quoting the final paragraph of the above paper and then passes on to consider the views expressed.

He holds that Drs. LOW and MANSON-BAHR are not justified in assuming that because approximately the same total of embryos is found in certain samples of blood, whether the patient lives normally or reverses his habits, there is daily migration and reappearance of the same undamaged embryos as against the author's (Clayton Lane's) view of regular death of embryos and fresh parturition by the adult females. He mentions that the number of ova in the faeces of a patient with hookworm infestation may be roughly the same day by day although there is no analogous possibility of migration and reappearance.

Another point on which stress is laid is that the normal midnight swarm of embryos occurring at Calcutta (whence the patient came) was found to be the same at Greenwich; *i.e.*, the periodicity had changed with the change in local time and latitude—why then should change of habits be regarded as a circumstance to alter periodicity?

As regards the guineapig experiment Clayton Lane notes the work of MURGATROYD who injected the embryos from man to man and remarked on the same rapid disappearance [in this case, of course, the organs could not be examined, so the remark as to the pathological uniqueness of the result may still hold good]. This certainly disposes of the theory of the cause being [species] incompatibility of blood.

FÜLLEBORN'S experiments are related and commented upon. These went to show that the numbers of embryos in different parts of the circulation were not the same in life (or just before death) as shortly after death.

The author then gives an account of some *ad hoc* experiments by Professor C. K. DRINKER and Dr. Madeleine FIELD of Harvard University showing that lymph flow may continue for more than 1½ hours after sudden death from potassium cyanide poisoning. Accordingly the finding of lymph-borne microfilariae in the right heart and lungs after death from cyanide is no proof that they were there at the time of death.

To the statement "why embryos should be able to hold their own against the currents of blood in the heart and large vessels is not clear, but it is a fact that they do" as LOW and MANSON-BAHR have written, and that they may do this by virtue of a spicule and surrounding

papillae, Clayton Lane replies that more modern technique shows that there is no spicule and that they thereby maintain their position is consequently not a "fact."

The analogy with *Dirofilaria immitis* to which Low and MANSON-BAHR refer as regards their capability of withstanding the force of the blood-current is not valid, for here it is the adults which wind round the columnae carneae and so maintain their position in the rush of the circulation, and not embryos as in the case of *W. bancrofti*.

Five years ago Clayton Lane concluded that the periodicity must be due to simultaneous parturition of the adult female filariae and O'CONNOR's findings that in the same cases (and he examined a number) all the female worms were at the same stage of pregnancy at the time of death of the subject and that the cycle is such that under "normal" conditions parturition occurs about midday support this view. [Many readers will call to mind the Meeting of the Royal Society of Tropical Medicine and Hygiene at the end of 1933 when slides were shown of females filled with embryos at noon, but with collapsed and emptied uteri in the cases of those removed two hours later.]

The author from a study of O'CONNOR's slides and of what is known of the subject concludes that there occur "in this periodic filariasis two parallel cycles each of 24 hours' duration (the first a cycle of intra-uterine development ending with parturition normally about midday, the second the well-known one of the swarming of microfilariae in the blood with its apex about midnight) and that it is merely unreason which after independent confirmation will refuse to connect them as cause and effect." The question of the *site* of the "daily destruction of embryos which must accompany a periodicity due to timed parturition" is one which may more fittingly be taken up after simultaneous parturition has been confirmed.

H. H. S.

HINMAN (E. Harold), FAUST (Ernest Carroll) & DEBAKEY (Michael E.).
Filarial Periodicity in the Dog Heartworm, *Dirofilaria immitis*, after Blood Transfusion.—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1043-1046.

"It is apparent that, in the case of the dog heartworm infection, periodicity cannot be explained on the basis of cyclical parturition and daily destruction of larvae."

The worm considered is *Dirofilaria immitis*. Recent work on periodicity is considered. The experiment consisted in importing, apparently to New Orleans from Chicago (well outside the endemic area) a dog weighing 12 lbs. which was then kept in a double screened cage. On 29th March a third of its blood was removed and the same quantity of blood from a heavily infected donor injected, the donor being compensated by injection of the citrated blood of the recipient. Before the exchange the donor's blood showed a maximum of 47,000 microfilariae* at 3 a.m. and a minimum of 16,000 at 7 a.m., and after it a maximum of 19,875 at 5 p.m. and a minimum of 6,000 at 7 p.m. The numbers at 5 p.m., which had been 21,400 before the exchange, rose from 6,875 on the 31st March to 44,500 on the 4th of May. The recipient had no microfilariae before the receipt of blood containing 27,475 of them per cc. of donor's blood. After the bloods had become evenly mixed this should have given about 9,000, but only 8 per cent.

* All numbers per cc.

of this number ever appeared in the peripheral blood, the maximum figure immediately after the injection being 750 at 7 p.m. and the minimum 175 at 3 a.m. Thereafter at 5 p.m. the maximum of 750 was counted on 13th April and the minimum of 50 on the 4th of May. "Daily production and destruction of the microfilariae would have returned the count to normal levels within 24 hours" for injection of sodium citrate, of unstated quantity, was shown to produce no apparent reduction in numbers of microfilariae. "The fact that the majority of embryos disappeared almost immediately after transfusion into the recipient may be due to their filtration by the viscera, particularly the lungs as suggested by Fülleborn." C. L.

TISSEUIL (J.). Processus de destruction des microfilaries vivantes par l'épiploon chez la saignée philander. [**Destruction of Microfilariae in an Opossum by the Omentum.**—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 735-737.

This report from the Institute of Hygiene, Cayenne, French Guiana, describes the condition found in the great omentum of an opossum which had infection with a filaria and a trypanosome.

The creature had when seen a gaping wound in the head, in the exudation from which were found microfilariae and trypanosomes. Neither is described. The omentum was nodular from numerous yellowish granulations mostly very small, but a few large and showing encysted adult filariae. The latter on section displayed a wall containing many pigmented cells, many vacuolated cells and a few giant cells. The early cysts containing microfilariae showed masses of these, entire and moving but not progressing, and were lined by a flattened endothelium, the fluid showing few leucocytes, mostly mononuclear. As to their fate, the cyst wall thickens progressively by appearance of giant cells among large mononuclear and a few polynuclear cells, the cyst cavity lessens progressively in size and microfilariae become progressively fewer and show fragmentation, till there is left a double walled granulation surrounding a central vessel clothed with giant and mononuclear cells. It is suggested that the microfilariae group themselves round blood vessels in the attempt to enter them, some penetrating, the rest being immobilized in the cysts. C. L.

Low (G. Carmichael). **The Skin Conditions found in *Loa loa* Infections.**—*Jl. Trop. Med. & Hyg.* 1934. Dec. 1. Vol. 37. No. 23. pp. 359-360.

The skin conditions found in, and the diagnosis of, loa infection is considered.

Calabar swellings, a term first used by THOMPSTONE of Southern Nigeria, were believed by MANSON to be due to parturition by the female worm because he found microfilariae in fluid obtained by puncturing such a swelling. His patient, however, had embryos in the blood. Low's control, in which a swelling was punctured in one who had no microfilariae in the blood, showed no embryos in the swelling. Low believes the swellings to be due to liberation of toxins from a dead worm. The other skin manifestations dealt with are pruritus, explicable by the presence of the parasite just under the true skin, and giant urticaria perhaps due to some personal idiosyncrasy. Diagnosis of loa infection is by seeing or extracting the worm, seeing embryos in the peripheral blood, the presence of Calabar swellings, unexplained eosinophilia, and Fairley's skin test. C. L.

BAMUNDAGA (D.). An Unusual Case of Dracontiasis.—*East African Med. Jl.* 1934. Dec. Vol. 11. No. 9. pp. 292-293.

The opening was over the lower angle of the left scapula, and the worm extended over the left clavicle. There were, it is held, two worms described as fused together for the first two inches. C. L.

BRUMPT (E.), DUVOIR (M. E.) & SAINTON (J.). Un cas de cénurose humaine dû au *Coenurus serialis* parasite habituel des lapins et des lièvres.—*Ann. Parasit. Humaine et Comparée.* 1934. Sept. 1. Vol. 12. No. 5. pp. 371-383. With 8 figs. [15 refs.] [See this *Bulletin*, Vol. 31, p. 787.]

CASTELLANI (Aldo). Elephantiasis nostras. (Non-Filarial Elephantiasis).—*Jl. Trop. Med. & Hyg.* 1934. Sept. 1. Vol. 37. No. 17. pp. 257-264. With 4 text figs., 1 chart & 30 figs. on plates. [See this *Bulletin*, ante, p. 73.]

CAVSTON (F. G.). Neostam in the Treatment of Bilharzia Disease.—*Jl. Trop. Med. & Hyg.* 1934. Oct. 15. Vol. 37. No. 20. pp. 316-317.

CAWSTON (F. Gordon). The Treatment of Bilharzia Diseases by Antimony Potassium Tartrate, with the Consideration of Claims advanced for Other Remedies.—*Jl. Trop. Med. & Hyg.* 1934. Dec. 15. Vol. 37. No. 24. pp. 385-386.

CHEN (H. T.). Reactions of *Ctenocephalides felis* to *Dipylidium caninum*.—*Ztschr. f. Parasitenk.* 1934. July 21. Vol. 6. No. 5. pp. 603-637. With 2 diagrams & 29 figs. on 4 plates. [3 pages of refs.]

GALLARDO (Vicente P.). Anthelmintics in General Practice.—*Jl. Philippine Islands Med. Assoc.* 1934. Sept. Vol. 14. No. 9. pp. 350-353.

GIRGES (Rameses). The Clinical Aspect of Ascariasis.—*Jl. Trop. Med. & Hyg.* 1934. Dec. 15. Vol. 37. No. 24. pp. 387-392.

HAUTEFEUILLE (J.). Méningite vermineuse.—*Ann. Parasit. Humaine et Comparée.* 1935. Jan. 1. Vol. 13. No. 1. pp. 21-27. With 1 chart. [12 refs.]

LEATHERS (W. S.) & KELLER (A. E.). An Analysis of the Hookworm Problem in Mississippi.—*New Orleans Med. & Surg. Jl.* 1935. Jan. Vol. 87. No. 7. pp. 425-433. With 3 maps & 3 graphs. [14 refs.] [See this *Bulletin*, Vol. 31, p. 795.]

LOPEZ-NEIRA (Carlos). Terapeutica de las helmintiasis intestinales.—*Medicina Paises Calidos.* Madrid. 1934. Oct., Nov. & Dec. Vol. 7. Nos. 10, 11 & 12. pp. 470-485; 497-528; 545-586. [8 pages of refs.]

MARCHAL (G.), SOULIÉ (P.) & GRIGAUT (A.). Néphrose lipidique et helminthiase.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Dec. 24. 3rd Ser. 50th Year. No. 34. pp. 1721-1726.

MONTEL (Lucien). Etude statistique sur le parasitisme intestinal basée sur 7,900 examens coprologiques.—*Marseille-Méd.* 1934. May 5. Vol. 71. No. 13. pp. 582-597. With 1 chart. [30 refs.]

TOSONOTTI (Tito). Sopra un caso di cosidetta "appendicite verminosa".—*Policlinico.* Sez. Prat. 1934. Nov. 5. Vol. 41. No. 44. pp. 1726-1732.

YELLOW FEVER.

- i. JAMES (S. P.). Renseignements concernant la fièvre jaune reçus pendant les six mois se terminant au 30 septembre 1934. [*Information concerning Yellow Fever received during the Six Months ending 30th September, 1934.*]—*Bull. Office Internat. d'Hyg. Publique.* 1934. Dec. Vol. 26. No. 12. pp. 2096–2102. With 1 map.
- ii. PRIDIE (E. D.). Résultats des récentes recherches sur la fièvre jaune au Soudan Anglo-Egyptien. [*Recent Investigations on Y. F. in the Anglo-Egyptian Sudan.*]—*Ibid.* pp. 2103–2105.
- iii. BOYÉ. Cas probables de fièvre jaune à Port Gentil (Gabon). [*Probable Cases of Y. F. at Port Gentil (Gabon).*]—*Ibid.* pp. 2106–2107.
- iv. JORGE (Ricardo). La fièvre jaune africaine. [*African Yellow Fever.*]—*Ibid.* pp. 2108–2122. [11 refs.]
- v. MOUCHET (R.), VAN HOOFF (L.), DUREN (A.), FORNARA (L.), CLAREBOUT (G.), HENRY (E.) & HENRARD (C.). Enquête sur l'endémicité amarile au Congo Belge en 1932–1933. [*Endemicity of Y. F. in the Belgian Congo during 1932–1933.*]—*Ibid.* pp. 2123–2135. With 1 folding map.
- vi. BOYÉ. Application en Afrique Occidentale Française du procédé de vaccination de Laigret contre la fièvre jaune. [*The Application of Laigret's Method of Vaccination against Y. F. in French West Africa.*]—*Ibid.* pp. 2136–2139.
- vii. PIERCE (C. C.). Epidémiologie et données scientifiques nouvelles concernant la fièvre jaune. [*Epidemiology and New Scientific Information concerning Y. F.*]—*Ibid.* pp. 2140–2141.
- viii. BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1934. Dec. Vol. 26. No. 12. pp. 2142–2145.—Rapport de la commission de la fièvre jaune. [*Report of the Y. F. Commission.*]

i. The author deals chiefly with protection tests and vaccination. He briefly summarizes the results of protection tests in various parts of Africa, and also in Brazil, and directs attention to their great importance from an epidemiological point of view. It is evident that there is still much to be learnt about this aspect of the disease and four recent observations are mentioned in this connexion:—the occurrence of outbreaks of yellow fever in rural districts in the absence of *Aedes aegypti*; the persistence of the infection for long periods without any obvious cases of the disease, in rural districts, after its disappearance from the large centres of population; the fact that hedgehogs are susceptible to the ordinary viscerotropic form of yellow fever; the problem whether or not the virus can persist in the internal organs after its disappearance from the blood, and the degree of fixity of the neurotropic strain of the virus.

Mention is made of the results obtained by FINDLAY in the serum-vaccination of 75 persons, using horse immune serum prepared by PETTIT and STEFANOPOULO in Paris. Eighteen of the patients received 0.3 to 0.4 cc. per kilo body weight and the others 0.2 cc. per kilo, in addition to the usual dose of virus. Of these 14 had reactions attributable to the virus and 38 or 50 per cent., suffered from serum reactions due to the foreign protein. From a study on 305 persons vaccinated in various ways, it is found that about 5 per cent. are abnormally susceptible to the virus. In order to avoid any serious reactions, FINDLAY recommends the injection of a considerable excess of antibodies and by using doses of 0.4 cc. per kilo of the horse immune serum has successfully vaccinated 35 persons without producing any reaction attributable to the virus. Unfortunately, there is the danger

of producing allergic reaction, and there were two cases of serum sickness among these 35 subjects.

ii. The author discusses the results of protection tests in the Anglo-Egyptian Sudan and shows that the distribution of positive sera agrees with the hypothesis that yellow fever came from the west. In the southern part of the Bahr-El-Ghazal, however, there is no evidence of its existence in recent times, whilst in the north, at Wau for example, the infection existed very recently. This absence in the south is attributed to the severe restrictions on any movements of population owing to the existence of sleeping sickness.

The first case of yellow fever in the Sudan to be diagnosed pathologically has been found at Wau, where the liver of a man who died in July, 1934, showed the characteristic lesions. The clinical history of the case agreed with this diagnosis.

iii. Evidence is produced in support of the view that in May, 1934, a small centre of yellow fever existed at Port Gentil. A French couple both became ill ten days after their arrival and the husband died, both cases being diagnosed as alimentary intoxication. An examination of the blood of the widow showed that it contained protective antibodies against yellow fever. It is of interest that the results of protection tests in Port Gentil seemed to indicate that the disease had been absent for at least 12 years, as 19 sera of children aged 7 to 12 were all negative.

iv. An interesting discussion of the yellow fever problem with special reference to the possibility of its spreading to fresh localities. It is aptly pointed out that the disease has fallen from its importance as a world menace for since the discovery of the method of transmission every recent epidemic has been suppressed. With regard to the actual number of cases diagnosed as yellow fever, in 1933 there were only 52 in Africa and 14 in Brazil; and in the first nine months of 1934, 23 in Africa and 10 in Brazil. Consequently the author is of the opinion that the disease is on the decline, almost on the verge of extinction, and there is no foundation for the pessimistic views that are sometimes advanced as to its dangers.

v. A detailed account of the results of mouse protection tests in the Belgian Congo, from which it would seem that although the endemicity is wider than was realized, conditions do not favour the development of yellow fever epidemics. Nevertheless the presence of a certain degree of endemicity shows that it is necessary to augment the inspection of European centres and also to guard against the increased possibilities in the spread of the disease afforded by modern methods of communication.

vi. An account of LAIGRET's vaccination of 3,196 subjects in French West Africa [see below, p. 285].

vii. A brief summary of various observations on yellow fever, or its vectors, containing nothing new.

viii. The results of mouse protection tests in Africa are summarized as follows:—

In British West Africa out of more than 7,000 sera, 25 per cent. were positive; in French Niger, 22 per cent.; in Dahomey, 30 per cent.; in the Anglo-Egyptian Sudan from 0 to 16 per cent. In the Belgian Congo no positive cases occurred south east of a line from Dilolo to Albertville. In French Equatorial Africa all the territories were found positive. In Angola only a few localities were positive. The Commission reaffirms its confidence in the value of the mouse protection test

and the importance of continuing these investigations. But there is a divergence of opinion as to whether or not the presence of positive sera necessarily indicates the existence of clinical yellow fever. The histological examination of the liver obtained either by the viscerotome or after autopsy is recommended in the cases of all fatal febrile infections of less than 10 days duration occurring in suspected endemic areas.

With reference to vaccination, the Commission urges the importance of following the history of all vaccinated subjects in order to decide the relative value of the two methods at present in use. *E. Hindle.*

BEEUWKES (Henry), MAHAFFY (A. F.), BURKE (A. W.) & PAUL (J. H.).
Yellow Fever Protection Test Surveys in the French Cameroons, French Equatorial Africa, the Belgian Congo, and Angola. *Trans. Roy. Soc. Trop. Med. & Hyg.* 1934 Nov. 27. Vol. 28. No. 3 pp. 233-258. With 4 maps.

Details are given of the results of a yellow fever protection test survey covering the examination of 4,428 specimens in 108 towns of the French Cameroons, French Equatorial Africa, the Belgian Congo, and Angola.

Results of similar studies have been previously published by the Belgian Mission, and also by BOYÉ and JORGE [this *Bulletin*, Vol. 31, pp. 831-832]. Except in French Equatorial Africa the percentages of positive sera were much lower than in West Africa proper, probably owing to the fact that conditions in these regions are relatively unfavourable to the maintenance of yellow fever infection. Although extensive epidemics have occurred both recently and in the past, at present endemicity seems to be excluded throughout this entire region.

In French Equatorial Africa 1,643 specimens were examined and 18.4 per cent. were positive, but no case of yellow fever has ever been reported from the Colony in spite of the fact that the protection tests indicate that extensive epidemics of the disease must have occurred within recent years. High percentages of positive sera were obtained in many towns in the interior including several near the border of the Anglo-Egyptian Sudan. The findings in the coastal area indicate that the incidence during recent years has been almost negligible.

In the French Cameroons only 3.6 per cent. were positive in 496 specimens collected in nine towns. The children were almost completely negative and the specimens from adults showed a fair percentage of positives in only two towns.

The survey in the Belgian Congo included the examination of 1,740 specimens from 43 towns, and 8.8 per cent. of these were positive. The interior seems to have been completely free from yellow fever during recent years, but has experienced the disease in the past. The results in towns along the Congo and Oubangui rivers suggest the possibility of the infection being carried into the interior of French Equatorial Africa by river traffic.

The results of the examination of 949 specimens from Angola showed only 11 positive, and the practically negative findings in the south and south-eastern portions of the Belgian Congo and throughout Angola, indicate that the limits of yellow fever invasion in these directions have been reached.

[The results recorded by JORGE (this *Bulletin*, Vol. 31, p. 832) seemed to indicate that 44 out of 950 sera from Angola were positive.

These figures were derived from the author's table (p. 1402) giving a summary of the results, in which the *percentages* of positive and doubtful sera were totalled, giving the erroneous impression of an incidence four times higher than was actually the case.] *E. H.*

RECIO (A.). Absence d'immunisines anti-amariles chez les Cubains nés après la disparition de la fièvre jaune. [**The Absence of Yellow Fever Immune Bodies in Cubans born since the Disappearance of the Disease.**]*—Bull. Acad. Méd.* 1934. Nov. 6. 98th Year. 3rd Ser. Vol. 112. No. 35. pp. 543-546.

By means of the mouse protection test the author has examined specimens of serum collected from 27 white and 14 coloured Cubans. The results are given in tabular form and show that 12 out of 16 persons born previous to 1901 contained antibodies against yellow fever, but the sera of the 25 subjects born subsequent to this date gave uniformly negative results. *E. H.*

DUDLEY (Sheldon F.). **Can Yellow Fever spread into Asia? An Essay on the Ecology of Mosquito-Borne Disease.***—Jl. Trop. Med. & Hyg.* 1934. Sept. 15. Vol. 37. No. 18. pp. 273-278. [18 refs.] Also in *Jl. Roy. Nav. Med. Serv.* 1935. Jan. Vol. 21. No. 1. pp. 16-28. [18 refs.]

An interesting speculative essay on the possibilities of yellow fever spreading into Asia.

The author directs attention to the nature of the sea-borne traffic between East Africa and Asiatic ports, which is largely conducted by Arab dhows and coasting sailing vessels, as primitive as ever were the old sailing ships which carried yellow fever across the Atlantic. These sea-lanes should be as easy for the disease to travel by as was ever the old "middle passage" from West Africa to the Caribbean Sea in the past.

A comparison of the geographical distributions of *Aedes aegypti*, dengue and yellow fever, respectively, suggests that the races of *A. aegypti* east of longitude 20, while remaining good carriers of dengue become inferior vectors of yellow fever [but see below, p. 292]. Although there may be biological differences between the races of *A. aegypti* in various parts of the world, as suggested by certain transmission experiments and supported to some extent by epidemiological evidence, it is aptly pointed out what little things may upset the balance of Nature, and it is conceivable that an increase in the rapidity and amount of mechanical transport might compensate for a hypothetical inferiority of the potential local vector, or even allow the West African races of yellow fever mosquitoes to gain ascendancy over the races to the east of them and extend their range into Asia. It is of the greatest importance, therefore, that sanitary and ships' medical officers should do all in their power to improve, encourage and enforce any measures which will hinder "yellow Jack" in travelling eastward from his stronghold in Central Africa.

This valuable article contains in addition many well-chosen examples of the epidemiology of insect-borne diseases, and should be read in its entirety by those interested in the subject. *E. H.*

NICOLLE (Charles). L'infection inapparente, forme naturelle d'extinction de certaines maladies infectieuses. [**Non-Evident Infections, a Natural Stage in the Disappearance of Certain Infectious Diseases.**]—*Arch. Inst. Pasteur de Tunis*. 1934. Dec. Vol. 23. No. 4. pp. 438-440.

The author sees in the results of protection tests for yellow fever in the Anglo-Egyptian Sudan [this *Bulletin*, Vol. 31, p. 833], a demonstration of the existence of a disease which has ceased to produce any clinical signs of its presence, but can still be detected by the protective antibodies that are found in the serum. It is considered that this is a very good example of the final stage in the extinction of an infectious disease, an interesting hypothesis developed by the author in his essay "*Destin des maladies infectieuses*," published by F. Alcan, Paris.

E. H.

MATHIS (C.). Pouvoir protecteur exercé vis-à-vis du virus amaril de souris par le sérum du sujet ayant fourni la souche française du virus de la fièvre jaune. [**The Protective Action against Mouse Yellow Fever Virus of the Serum of the Patient who furnished the French Strain of Virus.**]—*Bull. Acad. Méd.* 1934. Oct. 23. 98th Year. 3rd Ser. Vol. 112. No. 33. pp. 338-340.

The French strain of yellow fever virus was originally obtained in 1927 from a mild case of the disease in a young Syrian at Dakar [see this *Bulletin*, Vol. 25, p. 538]. After an interval of about 7 years the author examined the serum of this subject by means of protection tests in mice, and found that it contained antibodies against the mouse virus, though only to a slight degree.

E. H.

STEFANOPOULO (G. J.) & MOLLARET (P.). Hémiplegie d'origine cérébrale et névrite optique au cours d'un cas de fièvre jaune. [**Hemiplegia of Cerebral Origin and Optic Neuritis in the Course of a Yellow Fever Case.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1934. Nov. 19. 3rd Ser. Vol. 50. No. 29. pp. 1463-1465.

The possibility of ordinary yellow fever virus showing neurotropic affinities is supported by the authors' account of a patient who developed hemiplegia and other nervous symptoms following an attack of yellow fever. The authors produce convincing evidence in support of the view that the nervous lesions were the result of the yellow fever, and insist on the danger of nervous complications in using neurotropic virus for vaccination. Consequently they advocate the use of combined virus and immune serum for this purpose instead of virus alone.

E. H.

MATHIS (C.), LAIGRET (J.) & DURIEUX (C.). Trois mille vaccinations contre la fièvre jaune en Afrique Occidentale Française au moyen du virus vivant de souris, atténué par le vieillissement. [**Three Thousand Vaccinations against Yellow Fever in French West Africa, by Means of Living Mouse Virus, attenuated by Age.**]—*C. R. Acad. Sci.* 1934. Oct. 15. Vol. 199. No. 16. pp. 742-744.

The authors have submitted a total of 3,196 Europeans in French West Africa to the method of vaccination involving three inoculations of living mouse virus attenuated by age, in the same way as the spinal cords of rabbits infected with rabies.

The infected mouse brains were attenuated for one, two and four days respectively and then dried *in vacuo*. Appropriate doses of the dried material were made up in ampoules and used for inoculation. The treatment consisted of three inoculations at intervals of 20 days, first of the virus attenuated for 4 days, next of the 2-day virus and finally of that attenuated only one day.

According to the authors no local reaction has ever been observed, but about one-third of the subjects showed a febrile reaction after the first, less frequently after the second, and very exceptionally after the third inoculation. The reaction developed 6 days after the inoculation and was accompanied by fever, headache, and pain in the orbit and back, which lasted from 12 to 30 hours. Two cases presented more severe symptoms, one a meningic syndrome and the other a myelitis with a transitory paraplegia. They both recovered, however, and neither the blood nor the cerebrospinal fluid was infective to monkeys or mice.

Among those vaccinated in Senegal, 70 per cent. acquired immunity after the first inoculation but three inoculations are recommended. Nevertheless, the authors mention that cases of yellow fever [numbers not stated] have occurred in patients at least 20 days after the third inoculation, so the method is not infallible. E. H.

LAIGRET (J.). Résultats d'une mission effectuée en A.O.F. pour l'organisation de la vaccination contre la fièvre jaune. [**The Results of a Mission in French West Africa for the Organization of Vaccination against Yellow Fever.**—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 813-816.

— La vaccination contre la fièvre jaune (quatrième mémoire). Sur une mission pour l'application de cette vaccination en A.O.F.—*Arch. Inst. Pasteur de Tunis.* 1934. Dec. Vol. 23. No. 4. pp. 413-437.

The author gives a brief summary of the method of vaccination recommended by him, namely three inoculations of attenuated mouse virus, suspended in glycerine [see this *Bulletin*, Vol. 31, p. 79], and gives the results of applying the method for the protection of more than 3,000 subjects in French West Africa. Since the inoculations seem to have been attended without any accidents, except nervous symptoms in two cases which both recovered, the establishment of a centre in France is advocated, so that persons could be vaccinated under favourable conditions and acquire immunity before arriving in the endemic areas. For the present the Pasteur Institute at Tunis will continue to prepare the vaccine, and will send it to Paris, where the inoculations will be made gratuitously at the Pasteur Hospital by Dr. René MARTIN. Since yellow fever vaccination by the use of virus and immune serum is also practised at the same hospital, the author asks that any person wishing to have virus alone should demand the "Method of the Pasteur Institute, Tunis." E. H.

FINDLAY (G. M.). **Immunisation against Yellow Fever with Attenuated Neurotropic Virus.**—*Lancet.* 1934. Nov. 3. pp. 983-985. [17 refs.]

The author gives the results of inoculating rhesus monkeys with attenuated virus as used by MATHIS, LAIGRET and DURIEUX in their mass experiments in West Africa.

Six monkeys were inoculated subcutaneously with 1 cc. of a 1 in 100 dilution of infected mouse brain, attenuated by an exposure of 4 days at 20°C. Four of these monkeys showed virus in the peripheral blood stream and developed immunity; the remaining two remained negative but did not develop any immunity. On receiving the second inoculation of mouse virus, attenuated for 2 days, these two monkeys both showed virus in the blood and subsequently became immune. An additional four monkeys were inoculated with only 0.5 cc. of the 4-day vaccine. Three showed virus in the blood and one of these developed encephalitis after 12 days and virus was found in large quantities in its brain. The fourth monkey showed no virus in its blood and did not develop immunity.

These results support the view that the development of immunity is correlated with the circulation of living neurotropic virus in the peripheral blood stream and emphasize the danger of using this method of vaccination for human immunization. The barrier between the blood stream and the brain may be broken down and the central nervous system invaded by the virus, as seems to have been the case with two of the persons vaccinated by LAIGRET [above]. Moreover it is well known to occur in mice and guineapigs inoculated with the neurotropic virus as well as in monkeys. A further danger is the possibility of the neurotropic virus suddenly reverting to the viscerotropic form, for experiments with hedgehogs [see below, p. 290] show that the mouse virus should be regarded as pantropic rather than strictly neurotropic.

Finally, the presence of active neurotropic yellow fever virus in the blood during the course of vaccination renders the patient a potential danger both to himself and the community if any of the known mosquito carriers of yellow fever are present, for it has been shown that *Aedes aegypti* is capable of taking up this virus from the blood of monkeys and transmitting it to other animals [see this *Bulletin*, Vol. 30, p. 355]. In view, therefore, of the dangers attending this method, the use of attenuated neurotropic virus for human immunization is not recommended.

E. H.

FINDLAY (G. M.). Immunisation contre la fièvre jaune au moyen de virus neurotrope vivant et d'immunsérum hétérologue. [**Immunization against Yellow Fever by Means of Living Neurotropic Virus and Heterologous Immune Serum.**—*Bull. Acad. Méd.* 1935, Jan. 22. 99th Year. 3rd Ser. Vol. 113. No. 3. pp. 78-95. [32 refs.]]

A good general discussion of the subject followed by an account of the results obtained in the immunization of 100 persons against yellow fever by means of inoculations of living neurotropic virus and heterologous immune serum prepared by PETTIT and STEFANOPOULO.

It is considered advisable not to use neurotropic virus after more than 150 passages in mice, as after 200 passages the neurotropism has a tendency to become augmented and, moreover, antigenic modifications may possibly develop and interfere with the development of immunity against the original virus.

The author emphasizes the dangers of using living virus attenuated in various ways, since the circulation of virus in the circulation constitutes a source of danger not only to the patient but also to the community in tropical countries where the transmitting agent occurs.

When, however, immune serum in sufficient quantity is injected any reactions due to the virus are checked, and at the same time virus does not circulate in the blood. The necessity for an adequate dose of immune serum is well exemplified in the history of 100 cases, 70 males and 30 females, who were vaccinated in this way. When less than 0.3 cc. per kilo. body weight of immune serum was used 15 out of 57 cases showed reactions which could be attributed to the action of the virus. The remaining 43 cases received injections of 0.3 to 0.4 cc. per kilo body weight and such reactions were suppressed. Approximately half of all the cases treated showed reactions due to the injection of the heterologous proteins. In 3 cases there was definite local oedema two hours after injecting the serum but in all the others the reaction appeared between the 3rd and 10th day. Only 9 subjects are stated to have shown symptoms of any importance. *E. H.*

LAIGRET (J.). **Immunisation against Yellow Fever. Vaccination and Sero-Vaccination.** [Correspondence.]—*Lancet*. 1935. Jan. 19. pp. 176-177.

A reply to the foregoing communications.

The author admits that the multiplication of the virus in the vaccinated organism is the essential condition in the development of immunity, but the intensity of this infection is so feeble that up to the present he has been unable to prove the virulence of the blood in any vaccinated persons. In the case of FINDLAY's monkeys, the relatively large dose inoculated is considered to be the reason why he was able to infect mice with their blood. With regard to the fear that the living vaccine transmitted by mosquitoes from vaccinated to non-vaccinated persons could communicate yellow fever, return to virulence has never occurred under the conditions of human vaccination. Reference is also made to unpublished experiments by the author in conjunction with MATHIS and DURIEUX. Each day for 20 days different batches of mosquitoes were fed on vaccinated persons and subsequently fed on unvaccinated persons and finally ground up and inoculated into rhesus monkeys. None of the men or monkeys showed any signs of any infection nor developed immunity. The risk of a meningeal reaction although real is considered to be very slight, in view of the fact that in more than 3,000 human vaccinations only two cases have been observed, and both recovered without sequelae. *E. H.*

MATHIS (C.) & MATHIS (M.). A propos de la vaccination contre la fièvre jaune. [**Vaccination against Yellow Fever.**]—*Bull. Acad. Méd.* 1934. Dec. 18. 98th Year. 3rd ser. Vol. 112. No. 41 pp. 817-820.

A polemical reply to FINDLAY's article on this subject [above].

The authors maintain that the publications cited do not support his conclusions that the attenuated virus may produce encephalitis in man and also that mosquitoes biting inoculated subjects may possibly become capable of transmitting yellow fever. The various publications, including the present authors' more recent experiments are summarized with the object of showing that there is no satisfactory evidence that neurotropic yellow fever virus can change into the viscerotropic form during a single passage. Moreover, 4,000 vaccinations by means of attenuated neurotropic virus have been practised in French West Africa without producing any signs of the disease. *E. H.*

DUREN (A.). Où en est la question de la vaccination contre la fièvre jaune. [**The Present Position of Vaccination against Yellow Fever.**]—*Bruxelles-Méd.* 1935. Jan. 13. Vol. 15. No. 11. pp. 300-303.

A general account of the subject.

E. H.

MATHIS (C.), DURIEUX (C.) & ADVIER (M.). La vaccination anti-amarile comporte-t-elle des dangers dans les régions où la fièvre jaune sévit endémiquement et où les "*Stegomyia*" abondent? (Première note.) [**Is Yellow Fever Vaccination Dangerous in Regions where the Disease is Endemic or where "*Stegomyia*" abounds?**]—*Bull. Acad. Méd.* 1934. Nov. 6. 98th Year. 3rd Ser. Vol. 112. No. 35. pp. 535-538.

Three patients were inoculated each with 1 cc. of a one per cent. suspension of neurotropic virus equivalent to 0.002 gm. of mouse brain, and none of them showed any reaction. The serum of each patient was subsequently tested in mice for its protective properties. The serum of one of them protected 4 out of 5 mice, the other two gave inconclusive results. Mosquitoes (*Aedes aegypti*) were fed on all three patients during the 6 to 8 days following the inoculation of the virus, and subsequently allowed to bite two *Macacus rhesus*, neither of which developed any signs of infection. One of these monkeys was also inoculated with the ground-up contents of these mosquitoes, also with negative results.

E. H.

DHONT (C. M.), SCHÜFFNER (W. A. P.) & SNIJDERS (E. P.). Over het gedrag van het neurotrope "virus fixe" der gele koorts bij caviae en rhesus-apeen. [**Action of the Neurotropic "Fixed Virus" of Yellow Fever in Guinea-pigs and Rhesus Monkeys.**]—*Nederl. Tijdschr. v. Geneesk.* 1934. Oct. 20. Vol. 78. No. 42. pp. 4826-4836. With 5 figs. on 1 plate. [10 refs.] English summary.

The first animal in which successful transmission of yellow fever from man was obtained was the monkey *Macacus rhesus*. That was a great step forward, but the possibilities of experimentation were greatly opened up when it was shown that the guinea-pig and the mouse were both susceptible animals.

In the present series of experiments the first attempt was to transmit the neurotropic virus, the mouse "fixed virus," to the guinea-pig. Infective material for the first inoculation in guinea-pigs was obtained from mice in the 183rd passage of the Dakar strain. One half a mouse brain in unfiltered suspension, diluted 1-500 in 1 per cent. peptone and in dose of 0.01-0.02 cc. per guinea-pig, was used in intracerebral injection. None of the animals died of shock and none within 24 hours, which contrasted strongly with earlier experiments. This satisfactory result is ascribed to the use of what was now a neurotropic instead of a viscerotropic virus and a smaller dosage. About 4 days after inoculation a definite rise of temperature occurred (average 40.2°C.), then a fall to normal and, before death, a collapse temperature of about 35°. Loss of weight was the other main sign of infection. As in mice, the pathological condition was one of encephalitis, which was shown histologically by the characteristic perivascular lymphocytic "cuffing" of the cerebral vessels. The guinea-pig brain virus could be identified as a true yellow fever virus by using the protection test with a known yellow fever immune serum and a control normal serum respectively. The virus could

also be transmitted from one guineapig to another in series and again back to the mouse without loss of pathogenicity. An experiment was carried out to show the transmissibility of guineapig virus to the monkey by intramuscular injection. There were no immediate symptoms but the animal fell sick after 20 days with apparent paralytic symptoms and died on the 25th day. Two monkeys were inoculated with blood and liver suspensions respectively intramuscularly from this one. Both sickened 21 days later and both recovered. These two monkeys were subjected to the bite of a group of infective *Aedes aegypti* mosquitoes (viscerotropic virus), but except for a rise of temperature in one of them to 40.6° were not otherwise affected although a control monkey bitten by the same mosquito died of yellow fever. The deduction made is that the inoculation of blood and of liver suspension respectively gave rise to a slight attack which was recovered from and that this rendered the monkeys immune to yellow fever. The neurotropic yellow fever virus can also be transmitted from mice by intramuscular injection to monkeys. The disease is more protracted than the usual septicaemic one and death may not take place for 3 weeks. A final experiment showed that intramuscular injection of the neurotropic virus in the monkey results probably in a temporary septicaemia which, however, is not demonstrable after the 3rd day. In this respect it contrasts with the viscerotropic virus.

Their results, say the authors, taken as a whole, accord very well with those of the American and French workers and may be regarded as confirmatory.

W. F. Harvey.

LLOYD (Wray) & MAHAFFY (A. F.). **The Use of Guinea Pigs in Tests of Immunity against Yellow Fever with Small Quantities of Serum.**—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 51–58.

The advantage of being able to obtain a neutralization or protection test with such minute amounts of serum as may be obtained from infants led the authors to test the possibility of using guineapigs in the same way as THEILER used mice [see this *Bulletin*, Vol. 28, p. 723].

The results of inoculating serum-virus mixtures intracerebrally into guineapigs are compared with those of protection tests in mice, and in a series comprising 116 sera gave correct results in 95 per cent. of the cases. For the test 0.05 cc. of a 0.5 per cent. neurotropic virus suspension was mixed with 0.15 cc. of the serum to be tested and then incubated at 37°C. for two hours.

E. H.

FINDLAY (G. M.) & CLARKE (L. P.). **Infection with Neurotropic Yellow Fever Virus following Instillation into the Nares and Conjunctival Sac.**—*Jl. Path. & Bact.* 1935. Jan. Vol. 40. No. 1. pp. 55–64. With 2 charts. [16 refs.]

The nasal instillation of neurotropic yellow fever virus in monkeys and mice was found to be followed by the development of encephalitis.

Virus also reached the peripheral blood stream in small quantities 72 hours after instillation in mice, after which it disappeared. In five out of six rhesus monkeys infected virus was present in the blood 48 hours after instillation but had disappeared by the 6th day. In the sixth monkey the virus appeared in the blood on the 5th day and disappeared on the 7th day.

The virus was present in the olfactory lobes of a monkey and in the cerebral hemispheres of mice 2 days after nasal instillation, and then spread generally throughout the brain. The instillation of virus in the conjunctival sacs of 20 mice was followed by the development of encephalitis in 8 individuals after an average incubation period of 10 days, whilst with nasal instillation 36 out of 50 developed encephalitis after an average period of 9 days. In a discussion of the possible routes by which the infection reaches the brain it is considered that whilst the direct extension of virus along the axones cannot be entirely excluded, there is considerable evidence to show that the perineural sheath spaces are a possible and probable means of spread.

It was found that 5 monkeys containing immune bodies in their blood were immune to nasal instillation of the virus. Twelve mice that had survived nasal instillation were inoculated intracerebrally with the virus and with one exception all developed encephalitis; therefore it would seem that these mice had escaped the previous exposure owing to non-absorption of virus from the mucosa of the naso-pharynx. E. H.

STEFANOPOULO (G.), MOLLARET (P.) & DESNOS (E.). Inoculation du virus de la fièvre jaune au Porc. [**The Inoculation of Yellow Fever Virus into the Pig.**].—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 816-820. With 5 figs. on 2 plates & 1 chart.

A young pig was inoculated intracerebrally with a neurotropic strain of yellow fever virus; four days later it showed a sudden rise of temperature and subsequently developed nervous symptoms with progressive paralysis and died on the 7th day, with typical symptoms of myelo-encephalitis. Nevertheless six mice inoculated with the cerebrospinal fluid, and a monkey and six mice inoculated with an emulsion of the brain of this pig remained uninfected, and the monkey subsequently was inoculated with virus and died of yellow fever.

A second pig was inoculated subcutaneously with a viscerotropic strain, then 4 weeks later with a neurotropic mouse strain, and finally with two more doses of the ordinary virus. Protection tests with the pig's serum were feebly positive 28 days after the first inoculation, but became strongly positive after the last two doses. The cerebrospinal fluid was also strongly protective. E. H.

FINDLAY (G. M.) & CLARKE (L. P.). **The Susceptibility of the Hedgehog to Yellow Fever. II.—The Neurotropic Virus.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 335-345. With 8 figs. on 2 plates.

The authors have previously recorded the susceptibility of the hedgehog to viscerotropic strains of yellow fever virus [this *Bulletin*, Vol. 31, p. 841] and in the present article show that this species is also susceptible to neurotropic strains injected intracerebrally, subcutaneously or intraperitoneally.

The symptoms develop in 6 to 11 days and are invariably fatal but, unlike what is found in other susceptible animals, at death virus is present not only in the brain, but also in the liver, kidneys, spleen and adrenals, though only rarely in the blood. Virus obtained from the organs of hedgehogs produces a fatal encephalitis in mice and even after 10 passages in hedgehogs behaved as a fixed neurotropic strain

and moreover did not acquire any increased capacity for producing visceral lesions. It can be passed through Seitz filters and is neutralized by known yellow fever immune sera.

The changes produced by the neurotropic strains in the hedgehog include very slight lesions in the central nervous system, but especially focal degeneration in the liver, with acidophilic necrosis of the cytoplasm, occasional intranuclear inclusions and infiltration with mononuclear and polymorphonuclear leucocytes. In the stomach there are petechial haemorrhages in the gastric mucosa. The characteristics of neurotropic and viscerotropic yellow fever virus in the hedgehog are shown in the table.

Characteristics of Neurotropic and Viscerotropic Yellow Fever Virus in the Hedgehog

	Viscerotropic strain.	Neurotropic strain.
	Incubation period in days.	
	4-7	6-11
	Distribution of virus in tissues at death.	
Blood	++	±
Brain	++	+++
Liver	+++	+++
Spleen	+++	++
Kidney	+++	++
	Lesions.	
Liver	General necrosis	Focal necrosis
Kidney	Extensive degeneration of tubular epithelium	Degeneration of occasional epithelial cells
Stomach	Black vomit and haemorrhages	Occasional small haemorrhages
Heart	Fatty degeneration	No lesions
Brain	No lesions	Slight increase in microglia; occasional perivascular infiltration and increased mononuclear reaction in meninges

E. H.

FINDLAY (G. M.), HEWER (T. F.) & CLARKE (L. P.). **The Susceptibility of Sudanese Hedgehogs to Yellow Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 413-418. With 4 figs. on 1 plate.

The results of these experiments show that Pruner's hedgehog from the Sudan is susceptible to yellow fever and the possibility of such a species acting as a reservoir for the virus cannot be ignored.

Four Pruner's hedgehogs (*Atelerix albiventris*=*Erinaceus pruneri*) from the Sudan were inoculated subcutaneously with viscerotropic yellow fever virus. The first two were inoculated, one with liver and the other with blood of a monkey infected with the Asibi strain; both died of yellow fever after 4½ and 9 days respectively. The third hedgehog, inoculated with a Berkefeld filtrate of the liver of an infected European hedgehog, died after 22 days and a monkey inoculated with the liver of this animal died of yellow fever 11 days later. This hedgehog had been kept at 50° to 60°F. and was in a semi-comatose condition for 15 days after inoculation. The prolonged duration of the disease in this individual may possibly be due to the

hibernating condition, for a European hedgehog kept at the same temperature also showed an incubation of 17 days when inoculated with yellow fever.

The fourth Sudanese hedgehog inoculated with a Seitz filtrate of the liver of the second one, did not die, although a European hedgehog inoculated with the same material died in 6 days. It was subsequently found to be immune. *E. H.*

MATHIS (Maurice). Biologie comparée, en conditions expérimentales, de quatre souches du moustique de la fièvre jaune. [**The Comparative Biology, under Experimental Conditions, of Four Strains of Yellow Fever Mosquitoes.**—*C. R. Soc. Biol.* 1934. Vol. 117. No. 35. pp. 878-880.]

The author compared four strains of *Aedes aegypti* obtained respectively from Athens, Cuba, Dakar and Java, with regard to the duration of the various stages in their development, and also the number of eggs in the first two batches to be laid.

All four strains resembled each other very closely, the hatching of the eggs being produced by the same microbial factors, the larval stage lasting from 6 to 8 days (at 28°C.), the adults emerging after a nymphal stage of 48 hours, and the females laying their eggs within 48 hours of a blood meal. Unlike *Culex pipiens* and *Anopheles maculipennis* there is no evidence of the existence of distinct races, and the author is of the opinion that *Aedes aegypti* is a very homogeneous species in all parts of the world and consequently is a potential source of danger for the transmission of yellow fever in all countries where climatic conditions are favourable. *E. H.*

MOLLARET (Pierre) & STEFANOPOULO (G. J.). Le liquide céphalo-rachidien lombaire et sous-occipital dans la fièvre jaune expérimentale du *Macacus rhesus*. [**Lumbar and Sub-Occipital Cerebrospinal Fluid in Experimental Yellow Fever in *Macacus rhesus*.**—*C. R. Soc. Biol.* 1934. Vol. 117. No. 37. pp. 1101-1103.]

Nine rhesus monkeys were inoculated subcutaneously with a viscerotropic (Asibi) strain of yellow fever and the cerebrospinal fluid was examined in each. In spite of the absence of nervous symptoms, in every case there was a leucocytic reaction in the fluid collected on the 2nd to the 4th day after inoculation, consisting entirely of lymphocytes, which rose in some cases as high as 150 elements, with an average of 30 to 60. The albumen content, Pandey's reaction and precipitation of colloidal benzoin showed no important changes.

In two other monkeys the inoculation was followed by the development of nervous symptoms and in one of these inoculated with a neurotropic strain, and which only showed signs of illness on the 15th day, there were marked changes in the cerebrospinal fluid as indicated in the following table:—

Albumen.	Leuco-cytes.	Pandey's reaction.	Colloidal benzoin.
Before inoculation 0.15 gm. ...	7.2	—	0000010000000000
15th day after „ 0.65 gm. ...	50.0	—	0000022200000000
18th „ „ „ 1.00 gm. ...	67.2	+	0000002222100000

Five monkeys inoculated into the nervous system with a neurotropic strain all showed reactions analogous to the preceding case.

A resistant monkey and also six immunized animals all showed a lymphocytic reaction when inoculated with yellow fever virus. In three out of four monkeys inoculated with a neurotropic strain the cerebrospinal fluid contained virus from the 3rd to the 11th day of the disease. Moreover it was positive in 3 out of 9 monkeys inoculated with a viscerotropic strain.

In vaccinated or recovered monkeys the cerebrospinal fluid develops protective antibodies, sometimes to a very high titre, and the results in general support the view that yellow fever virus has certain neurotropic affinities.

E. H.

NICOLAU (S.), KOPCIEWSKA (L.) & MATHIS (M.). Etude sur les inclusions de la fièvre jaune. [**A Study of Yellow Fever Inclusions.**] —*Ann. Inst. Pasteur*. 1934. Nov. Vol. 53. No. 5. pp. 455–508. With 36 coloured figs. on 1 double plate. [Refs. in footnotes.]

The present study is mainly an expanded account of the results previously published in a series of notes [see this *Bulletin*, Vol. 31, pp. 499, 842 & 843]. The authors' main conclusions, based on the examination of human cases of yellow fever, and also of monkeys, mice, guineapigs and rabbits infected in various ways, are that the real yellow fever inclusions are oxyphilic bodies without any internal structure, sometimes surrounded by a halo, occurring in the karyoplasm, which is somewhat rarified, but still preserves its staining properties.

The dimensions of the bodies vary from less than 1μ in diameter up to 3 or 4μ , and generally they are multiple in each cell. It is necessary to distinguish these bodies from the oxychromatic degeneration of the nucleus of the infected cell, the result of its death or injury. The yellow fever inclusion body is supposed to be a response of the nucleus to the invasion of the virus, each particle of which is supposed to be enclosed in a kind of envelope, with the object of preventing its multiplication. These bodies are found not only in the nervous system but also in other cells derived from the ectoderm, such as hepatic and endothelial cells, also endothelioid cells of the spleen.

The authors consider that the so-called neurotropic strains of yellow fever do not multiply exclusively in the nervous system, as the virus can be found in the circulating blood for some days after being injected into the peritoneal cavity. It is thus not strictly neurotropic in the same way as rabies, poliomyelitis or Borns's disease.

E. H.

HUGHES (T. P.). **A Partial Purification of Yellow Fever Virus through Adsorption and Elution.**—*Jl. Bacteriology*. 1934. Oct. Vol. 28. No. 4. pp. 401–413. With 3 charts.

By using the well-known method of adsorption on kaolin followed by selective elution with dilute ammonia the author has made preparations of "mouse" yellow fever virus possessing a high degree of activity and having a protein content at least 50 times less than can be demonstrated by chemical tests for protein.

A suspension of infected mouse brain in distilled water was centrifuged and the supernatant fluid passed through a Seitz filter. To 9 cc. of the resulting filtrate was then added 2.25 cc. of a 40 per cent. suspension of kaolin in distilled water and the mixture shaken for 1 hour at room temperature. The kaolin was then removed from the supernatant fluid and both tested for virus. The virus was found to have been completely adsorbed by the kaolin, from which it was released by the addition of N/10 and N/100 ammonium hydroxide solution, but not by weaker dilutions (N/1,000).

Further experiments using a glycerine-acetate non-toxic buffer system, showed that the virus was adsorbed throughout its range of survival from pH 6.5 to 10.0. One-tenth volume of kaolin was found sufficient to adsorb all virus from suspensions having a low protein content, but was not effective in suspensions containing 50 per cent. serum (about 2.5 per cent. protein). For satisfactory results the protein content should be kept low.

Experiments with varying concentrations of ammonia showed that N/100 NH_4OH was the optimal one for routine use, and two minutes elution was sufficient to release the virus from kaolin. The virus particles evidently behave differently towards kaolin than do serum proteins or other substances present in blood serum or brain extracts. They are more rapidly and completely adsorbed (within 15 minutes) and when so adsorbed are released by a lower concentration of ammonia. The partial purification of yellow fever virus seems to be accomplished with ease and rapidity by means of this method. E. H.

HOSKINS (Meredith). An Attempt to transmit Yellow Fever Virus by Dog Fleas (*Ctenocephalides canis* Curt) and Flies (*Stomoxys calcitrans* Linn.).—*Jl. Parasitology*. 1934. Sept. Vol. 20. No. 5. pp. 299-303.

Dog fleas, *Ctenocephalides canis* Curt., were fed on rhesus monkeys infected with yellow fever and then allowed to bite normal monkeys immediately afterwards and at intervals of 7 to 72 hours. In no case was infection produced by their bites, but by injecting the contents of these fleas into monkeys it was found that the virus survived for 7 hours in the gut but died out before the expiration of 18 hours.

In the case of the stable fly, *Stomoxys calcitrans* Linn., infection was produced by bites 6 hours after the infective blood meal, but not after 16 hours. The contents of these flies remained infective up to 42 hours after the meal but the injections of flies 48 and 72 hours after feeding did not produce yellow fever in normal monkeys. The fact that these flies will readily bite a new host immediately after being interrupted in feeding suggests that they may be potential carriers of some importance. E. H.

JOURNAL OF THE ROYAL NAVAL MEDICAL SERVICE. 1935. Jan. Vol. 21. No. 1. pp. 28-34. With 1 fig.—The Menace of Yellow Fever. By a Medical Officer, Royal Navy.

A general article on the subject, containing extracts illustrating the dangers of yellow fever in the past, and in particular an interesting

account of the organization of mosquito control service in Rio de Janeiro, which has been applied at all the larger Brazilian ports.

E. H.

GORDON (R. M.). **Notes on Yellow Fever, with Special Reference to the Possibility of its Recurrence in Sierra Leone. With a Foreword by the Director of Medical and Sanitary Services, Sierra Leone.**—1934. Dec. 20 pp. Freetown: Govt. Printer.

A useful summary of the main facts concerning yellow fever with special reference to the possibility of its recurrence in Sierra Leone. The information has been brought up to date and issued in pamphlet form as a book of quick reference for any Medical Officer who may be called upon to contend with an outbreak of the disease. *E. H.*

SNIJDERS (E. P.), POSTMUS (S.) & SCHÜFFNER (W.). On the Protective Power of Yellow Fever Sera and Dengue Sera against Yellow Fever Virus.—*Amer. Jl. Trop. Med.* 1934, Nov. Vol. 14. No. 6. pp. 519–545. [27 refs.] [See this *Bulletin*, Vol. 31, p. 840.]

RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

KEMP (Hardy A.), MOURSUND (W. H.) & WRIGHT (Harry E.).
Relapsing Fever in Texas. IV. *Ornithodoros turicata* Duges : a Vector of the Disease.—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 479-487. [10 refs.]

The authors give various notes on *Ornithodoros turicata*, with special reference to the transmission of relapsing fever in Texas.

The tick seems to be widely distributed in Texas, having been recorded from several localities, usually sandy caves, in the north and south central parts of the State. Its rôle in the transmission of the disease has been demonstrated experimentally by the production of infection in rabbits, monkeys and rats, by the bites of these ticks. When feeding the larvae attach themselves very quickly, and become engorged within 10 to 30 minutes, when they detach themselves and leave the host. The nymphs usually behave in the same way, but the adults generally remain attached for hours, even up to two days. Coxal fluid is secreted during the feeding but this fluid does not seem to carry the infection, as no spirochaetes could be found in it, and rats inoculated with the fluid remained uninfected. Moreover, infection was produced by the bites of ticks in which the coxal apertures had been sealed with collodion.

Ticks were killed and examined at intervals of 2 to 15 days after feeding on a rat heavily infected with the Texas spirochaete. The organisms were found to make their way to practically every organ of the body, large numbers being found especially in the connective tissue. Although hereditary infection had been recorded the authors, in three experiments, obtained negative results by the inoculation of rats with saline emulsions of eggs laid by infected ticks. *E. Hindle.*

SACHS (Albert). **Relapsing Fever in Chitral.**—*Jl. Roy. Army Med. Corps.* 1934. Oct. Vol. 63. No. 4. pp. 217-230. With 1 map in text.

The author has analysed the medical case sheets of 50 cases of human relapsing fever that occurred in Chitral during 1932 and 1933, and gives a general account of the disease.

It is caused by a spirochaete morphologically resembling *S. recurrentis*, and the fever in all respects conforms to the known types. It is generally very mild, however, and first attacks may be missed especially as the onset has a close resemblance to that of malaria, for which it has frequently been mistaken. The incubation period varies between 5 and 15 days.

With reference to transmission clinical evidence supports the view that both tick and louse-borne types are present. No cases have occurred during the Chitral reliefs, when large numbers of troops march along the Hindustan-Chitral road, but always camp in the open, and do not use the levy posts or employ coolies. The disease seems generally to be contracted at one of the levy posts along the Dir-Drosh section and as the cases occur mostly in the hot weather the evidence is more in favour of the tick-borne type. *Argas persicus* was found in large

numbers at one post where the disease was prevalent, and in addition examples of *Ixodes reduvius* and *Hyalomma aegyptium*. Bugs were found at all the posts.

No definite evidence as to immunity is available since no strains of spirochaetes are now obtainable in India. E. H.

VILLAIN (G.). Septième cas de fièvre récurrente hispano africaine observé en Tunisie. [**Seventh Case of Spanish-African Relapsing Fever observed in Tunis.**—*Arch. Inst. Pasteur de Tunis*. 1934. Dec. Vol. 23. No. 4. pp. 447-448.]

The record of a case of infection, presumably with *Spirochaeta hispanica*, in a native of Tunis, living about 10 miles north of Enfidaville. The course of the disease was typical and spirochaetes were found in the patient's blood, but a monkey and two guineapigs inoculated with blood containing rare spirochaetes on the 9th day of the disease, and also two guineapigs inoculated with lice from the patient, failed to show any signs of infection. E. H.

KLEINE (F. K.) & KRAUSE (M.). Die Rolle der Wanze bei der Verbreitung des Rückfallfiebers. [**The Role of Bugs in the Spread of Relapsing Fever.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Nov. Vol. 38. No. 11. pp. 486-487.]

The authors conclude that bed bugs can only play a very small part as a reservoir for relapsing fever, not to be compared with that of ticks or lice. [See ROSENHOLZ, this *Bulletin*, Vol. 24, pp. 685-7.]

Larvae of bed bugs were fed on mice infected with strains of both European and African relapsing fever. From the sixth day onwards 2 to 10 specimens were ground up after various intervals and inoculated into mice. Out of 300 bed bugs 4 per cent. were found to be infective at intervals up to 80 days after the meal of infected blood, but out of 150 adult bugs similarly fed and inoculated into mice after 6 days interval, none produced infection. In addition 3,000 larvae from infected parents were inoculated into mice with negative results.

E. H.

KROÓ (H.). Studien ueber Immunität und Chemotherapie bei neugeborenen und erwachsenen Tieren. Untersuchungen ueber die Spirochäteninfektion der Hühner. [**Immunity and Chemotherapy of Newly-Born and Adult Animals. Researches on Fowl Spirochaetosis.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Dec. 31. Vol. 84. No. 1. pp. 1-13.]

Adult fowls and one-day old chicks were inoculated intramuscularly with similar doses of fowl spirochaetes. In the adult birds the infection lasted only 3 to 5 days, whilst in the one-day old chicks it was much more prolonged, the birds remaining positive up to 16 days after infection (in one case 21 days).

When killed spirochaetes were inoculated no immunity developed in the one-day old chicks, whilst the adult birds developed a well marked resistance.

In spite of the favourable chemotherapeutic index for arsenobenzol in the treatment of fowl spirochaetosis, one-day old chicks inoculated with the maximum tolerated dose were not cured, for after a time

spirochaetes reappeared in the blood. Unlike the blood of adult fowls similarly treated, the serum of the infected chicks, inoculated with chemotherapeutic agents, had little or no spirochaeticidal property. This is said to be in accordance with the fact that the relapse strain was immunologically identical with the original strain. The prolonged duration of the infection, the failure of chemotherapy to effect a cure, the occurrence of relapses, and the absence of spirochaeticidal antibodies in the serum, are considered to have a common basis. However, one-day chicks after infection and treatment were resistant against reinfection in the same way as adult fowls. The development of spirochaeticidal antibodies and obvious immunity seems to be a process which varies at different periods in the life of the fowl. *E. H.*

GRILLO (J.) & KRUMEICH (R.). Experimentelle Untersuchungen ueber Misch- und Sekundärinfektion. V. Mitteilung: Ueber die Beeinflussung der experimentellen Naganainfektion des Meerschweinchens durch eine Mischinfektion mit der *Spir. usbekistanica* oder dem Spirillum der Rattenbisskrankheit (Sodoku), sowie durch chemische Substanzen, die eine Temperatursteigerung oder sonstige Stoffwechseländerungen bedingen. [**The Influence on Nagana Infection in Guinea-pigs of a Mixed Infection with either *S. usbekistanica* or the *Spirillum* of Rat-Bite Fever, also of Chemical Substances causing a Rise in Temperature.**].—*Zent. f. Bakt.* I. Abt. Orig. 1934. Oct. 5. Vol. 132. No. 7/8. pp. 385–403. With 2 figs. [22 refs.]

The authors find that mixed infection with either *S. usbekistanica* or *Spirillum minus* affects the course of the disease in guinea-pigs infected with *Trypanosoma brucei*, the life of the animals being prolonged and the numbers of trypanosomes appearing in the circulation considerably reduced. In mice, mixed infections did not influence the course of the disease.

When guinea-pigs infected with *Trypanosoma brucei* were injected with chemical substances that raised the body temperature, such as pyrifur and sulfosin, the length of life of the guinea-pigs was prolonged, even though the substances had no obvious trypanocidal action. Similar results were also obtained with iodisan and thyroïdin, other substances producing alterations in the general metabolism of the guinea-pigs.

Discussing these results and previous work on the subject the authors consider that in the case of mixed infections the effect of the second infection is to give an additional stimulus to the cells comprising the defence mechanism of the host, with the result that there is an increase in antibody formation against both infections and correspondingly the life of the host is prolonged. *E. H.*

LEVADITI (C.), VAISMAN (A.) & PAÏC (M.). Dissociation des fonctions de mobilité et de reproduction chez les spirochètes et les trypanosomes, au moyen du rayonnement total de la lampe à mercure. [**Dissociation of Motility and Reproduction in Spirochaetes and Trypanosomes by Means of the Total Rays of the Mercury Lamp.**].—*C. R. Soc. Biol.* 1934. Vol. 117. No. 30. pp. 357–361. With 1 chart. [13 refs.]

The authors have exposed the Brazzaville strain of *Spirochaeta duttoni*, the fowl spirochaete, and *Trypanosoma evansi*, respectively,

to the total rays from a mercury lamp of 500 watts at a distance of 40 cm. In each case exposure to the radiations for periods of 10 to 30 minutes destroyed the reproductive capacity of the organisms but did not affect their motility. *E. H.*

COLEMAN (George E.). **Relapsing Fever Problem of California.**—*Amer. Jl. Public Health.* 1934. Oct. Vol. 24. No. 10. pp. 1056-1061. [20 refs.]

A general review of the subject, with special reference to the author's own observations. *E. H.*

REVIEWS AND NOTICES.

STRONG (Richard P.), SANDGROUND (Jack H.), BEQUAERT (Joseph C.) & MUÑOZ OCHOA (Miguel). **Onchocerciasis with Special Reference to the Central American Form of the Disease.**—*Contrib. from Dept. of Trop. Med. & Inst. for Trop. Biol. & Med.* Harvard Univ. No. 6. pp. xiv+234. With 2 maps, 103 figs. & 6 plates. 1934. Cambridge, Mass: Harvard Univ. Press, London: Humphrey Milford, Oxford Univ. Press. [21s.]

This monograph comes from the Department of Tropical Medicine and the Institute for Tropical Biology and Medicine of Harvard University. Each part deals with that section of the subject in which the writer's special knowledge gives him special authority.

In Part II Sandground deals with the validity of the various species of *Onchocerca*. He has obtained an unrivalled collection of material from Strong's first Guatemalan expedition, and has compared it with much from a number of different sources. He considers the generic characters; as to those of species his criterion is this: "In order to establish a new species safely, it is necessary to point out constantly present, and if possible easily recognizable, zoological characters by which it may be distinguished from related forms." He concludes, first that *O. caecutiens* Brumpt, 1919, is a synonym of *O. volvulus* Leuckart, 1893; and further that, on the basis of his material, there must fall within the same species *O. flexuosa* (Wedl, 1856) of *Cervus elephas*, the red deer of Central Europe [which in that case becomes the valid specific name], *O. gibsoni* Cleland and Johnstone, 1910, from Australian cattle, and perhaps the lost *O. lienalis* (Stiles, 1892) if indeed it belongs to this genus. Moreover *O. indica* Sweet, 1915, is a synonym of *O. gibsoni*; *O. cervicalis* Railliet and Henry, 1910, is a synonym of *A. reticulata* Diesing, 1841; and *O. bovis* Piettre, 1912, is one of *O. gutterosa* Neumann, 1910.

In Part III Bequaert deals equally helpfully with the taxonomy of the Simuliidae of Guatemala. Three have been demonstrated to be transmitters of *Onchocerca*, namely *S. metallicum* Ballardi, 1859 which name takes precedence of *S. avidum* C. C. Hoffman, 1930; *S. callidum* (Dyar and Shannon, 1927) which displaces *S. mooseri* Dampf, 1927; and *S. ochraceum* Walker, 1861. A general survey, based on the literature, is made of the preadult stages of the Simuliidae, and apparatus is described by which the adult is bred from the larva. For this the essential requisite is that the water used shall flow at not less than 1.1 kilometres per hour. The optimum rate is 4.5 and the upper figure is at least 30. It is illusory to slow speed by damming a stream in the hope that breeding will then cease in it, for it will persist at the weirs. As to temperature, breeding is possible from just below the snow line to a hot spring at 30.6°C.

Muñoz Ochoa describes in Part IV the local geography, seasons, climate, population and its customs, and the epidemiological statistics of certain coffee plantations in which at different ages the infection rate varies from 10 to 60 per cent. in males and from 0 to 33 per cent. in females, and notes that newcomers never escape the bites of simulum.

In Part I Strong provides the cement for the narrative. The onchocerca area in Guatemala is a strip on the Southern slope of the central range, some 60 miles long and 20 miles wide by the shaded map, and varying from 2,000 to 4,500 feet in altitude; and in it the inhabitants of 4 coffee plantations have been examined, for it is in them with their shade trees that the infection is most prevalent. In that one, Moca, in which the housing and sanitation of the permanent staff is the best, there is an infection rate among them of 40 per cent., yet in another, Helvetia, which lies 20 miles outside the present limits of endemicity, and in which close examination has failed to reveal any infection, the geographical and climatic conditions were practically the same as in Moca—that is to say numberless steep valleys with more or less swiftly-flowing streams with simulium breeding abundantly in all of them, and a fertile volcanic soil 8 to 14 feet deep. All seem to have a floating as well as a permanent Indian working population. Accordingly the immunity of Helvetia, that is the absence there of infective simulium flies, remains unexplained, though it is suggested that such flies may be wind-borne, or carried as stowaways in the ears of animals. Unexplained also is the localization of nodules about the head. This can hardly be attributed to the settling down of infective larvae at the spot where the simulium bite occurred, for although as the photographs show these Indians are ordinarily well covered with clothing, yet when working the men may wear nothing but a loin cloth and a large woven palm hat, and simulium bites almost invariably out of doors and by day. Again comparison with the photographs illustrating HISSETTE's work on the Belgian Congo (this *Bulletin*, Vol. 30, p. 709) where, also, blinding onchocerciasis is prevalent, bears this out, for most of the persons there shown have the body largely bare; the expedition which Strong aims at making to this area should shed welcome light on the problem.

A full review of this monograph is impossible, but it is noteworthy that 11 per cent. of proved infections had no palpable tumours, so bringing the infection into line with that produced by *O. gibsoni* in the horse. Considerable space is suitably given to the ocular lesions, which occurred in 5 per cent. of cases only, and to the siting of microfilariæ in the eye. As to removal of tumours, cases are recorded where others have appeared nearby, but in this locality 4 per cent. of simulium flies were infected. On the other hand the removal of all onchocerca tumours in a population of about 1,000 led to a drop in the infection rate from 40 to 4.5 per cent. in one year. Such are some of the important facts displayed in a notable publication. Clayton Lane.

CRAIG (Charles F.) [M.D., M.A. (Hon. Yale), F.A.C.P., F.A.C.S., Colonel, U.S. Army, Retd., D.S.M., etc.]. **Amebiasis and Amebic Dysentery.**—pp. viii+315. With 54 figs. 1934. London: Baillière, Tindall & Cox, 7-8 Henrietta Street, Covent Garden, W.C.2. [22s. 6d.]

In this book the author presents his readers with a very good account of the modern conception of amoebiasis of man, which he defines as the invasion of the tissues by the pathogenic amoeba *Entamoeba* (spelt *Endamoeba* according to American custom) *histolytica* (not *dysenteriae* as some American writers would insist). He adopts the view that amoebiasis is not synonymous with amoebic dysentery, which he regards as an unfortunate term for it gives rise, in the minds of most

medical men, to the idea that dysentery is the most common symptom of amoebic infection, whereas in the vast majority of cases the symptoms are so mild that they are often attributed to some other cause. The author believes, however, that the presence of the amoeba in the intestine is definite evidence of intestinal lesions, for he is not one of those who thinks that *E. histolytica* can live harmlessly in the lumen of the intestine like *E. coli*. The carrier, though he shows no evident symptoms of infection and may never have had dysentery, yet definitely has intestinal ulceration, the symptoms of which can usually be detected if carefully looked for.

In connexion with the epidemiology of amoebiasis, the world distribution is discussed, while the methods of spread by food handlers, flies and other means are critically examined. The conclusion is reached that though infection is as a rule necessarily sporadic, there do occur from time to time, particularly when gross faecal contamination of the water supply occurs, veritable epidemics, the most recent and striking of which the author considers to be the Chicago outbreak. This is said to have resulted from direct communications between the pipes of the water supply and sewage system in one or more large hotels. In fact it was this outbreak, resulting in the discovery that amoebiasis is far more widespread in the United States than had been suspected before, that induced the author to write this book for the assistance of medical men who had had little previous experience of the disease.

The description of the causative amoeba *Entamoeba histolytica* and the various non-pathogenic amoebae with which it may be confused, the symptomatology and pathology of intestinal amoebiasis and the complications and sequelae which may follow is carefully done. On the subject of diagnosis it is suggested that an X-ray investigation of the condition of the intestine in symptomless carriers might throw light on the character and extent of the lesions in these cases. As regards the modern method of inspection of the lower part of the large intestine by the sigmoidoscope as an aid to diagnosis the author expresses some scepticism, for he contends that it is always possible to detect the amoeba by faecal examinations if these are properly carried out. Some authorities in this country may be inclined to disagree with the author in this for it seems that often time may be saved by sigmoidoscopy, which has enabled amoebae to be discovered in scrapings from an ulcer when faecal examinations had been consistently negative. On the other hand, it is clear that the instrument can give no information as to the condition of the intestine above the sigmoid flexure.

It is well known that the author has devoted much time to investigations on the complement fixation reaction as a test for amoebiasis, and in this book he has devoted a whole chapter to its consideration. The technique of carrying out the test and the method of preparing the antigen from cultures of *Entamoeba histolytica* are carefully described. Those who are interested in this subject will be grateful to the author for his clear account of the test, which has been elaborated mainly by himself. On the question of treatment the author's views appear to be sound. No extravagant claims are made for any particular line of action and the timely warning is given that there is no method of treatment which will eliminate infection with *Entamoeba histolytica* in every case.

Such are some of the features of this very interesting and useful book. It is well got up and has an adequate supply of illustrations, most of which are microphotographs of what must be very excellent prepara-

tions. Whether microphotographs are as good for instructional purposes as carefully executed drawings is an open question. However, in this case they seem to answer very well the purpose for which they are intended. There can be no doubt that the book is a good one, which can be recommended with confidence to medical men seeking information on the subject with which it deals. C. M. Wenyon.

BARRAUD (P. J.) [F.R.E.S., F.Z.S., F.L.S., Entomologist to the Malaria Survey of India, Indian Research Fund Association]. **A Practical Entomological Course for Students of Malariology.**—*Health Bull. No. 18, Malaria Bureau No. 9.* pp. viii+141. With 208 figs. on 18 plates. 1934. Delhi: Manager of Publications. [Rs. 1-10 or 2s. 9d.]

It is interesting to compare the arrangements made for teaching a subject in different parts of the world, and we welcome the present Bulletin which gives detailed information about a course on the entomological side of malariology. We understand that the class has been organized in its present form for about ten years at Karnal in the Punjab under the Malaria Survey of India, and that Captain Barraud has been in charge of the entomological teaching for six years. Teaching in entomology occupies the whole of the students' time for two weeks: the contents of the Bulletin are divided to provide 14 lectures and 14 periods of practical work.

It is evident that teachers in India experience the difficulty which is familiar in this country: the entomological teaching must start at the beginning, and it cannot be assumed that the student has any general knowledge of the structure or nature of insects. After introducing a few elementary fundamental facts, the teacher proceeds to an account of the structure of the adult and larva, certain parts of which are described in great detail. On this basis of anatomical knowledge the students are then taught to identify Indian species of *Anopheles* in the adult and larval stages. During the course of the fortnight, they also receive instruction in dissection and mounting, in observing the criteria of the age of a mosquito, and on the enemies and parasites of these insects. The class also goes collecting, and is shown how to find larvae and transport them, how to rear *Anopheles* from the egg, etc. Catching stations are also visited. A consideration of the precipitin test is, very rightly we think, not included in the entomological part of the course. The Bulletin contains a full list of necessary apparatus and of diagrams and relevant literature shown to the class from time to time. It contains also valuable notes on small but important points of method for use in the field or the laboratory.

The reader will discover that the course at Karnal deals very thoroughly with the Indian species of *Anopheles* and that much emphasis is given to the anatomical side of the subject. Your reviewer feels that some of the anatomy might be omitted. The student must certainly learn enough to understand a description of an *Anopheles* adult or larva so that he can identify it; but is he concerned with the Chaoborinae, the rotation of the terminalia, the empodium, tentorium, parabasal spines and other "beggarly rudiments"? In the course which is outlined in the Bulletin under review the anatomical lessons are taught very thoroughly, but one wonders whether the student realizes that all the preventive problems with which he has to deal centre round the live insect. If the opportunity ever occurred of

planning so full a course, our own inclination would be to reduce the anatomy to that which is necessary for the recognition of species. We should like to find more time for observing living mosquitoes and experimenting with them; the students might be made to expose larvae which they had identified to different types of water, or they might offer vessels containing different types of water to adult females in a cage. They should also make observations with wet and dry bulb thermometers on the resting places which are chosen or avoided by mosquitoes in nature or in captivity, and perhaps study the length of life of several species under different climatic conditions. Above all things they should give time to the study of the house-haunting habit, enumerating the females of different species found in different parts of a house or a stable (and here they might be introduced to simple statistical tests of significance). A course such as this would be difficult to organize, but it would tend to throw emphasis on the relation of species to malaria. We suggest that the time has come for the malarialogist to follow the modern zoologist, discarding much anatomical study and concentrating attention on the living creature.

P. A. Buxton.

MISSIROLI (Alberto) [Direttore della Stazione Sperimentale per la Lotta Antimalarica]. **Lezioni sulla epidemiologia e profilassi della malaria impartite agli allievi della R. Università durante l'anno scolastico 1933-34.** [Lectures on the Epidemiology and Prevention of Malaria.] Pubblicate a cura di B. AURELI, Bibliotecaria. —552 pp. With 156 figs., 37 graphs & 8 plates (6 coloured). 1934. Rome. Ditta Armani di M. Courier, Via Cesare Fracassini 60 [Lira 80.]

Professor Missiroli has done good service to students of malarialogy in collecting into a single volume the course of lectures on the Epidemiology and Prophylaxis of Malaria which he delivered at the University of Rome in 1933-34. The treatment of those parts of the subject of malarialogy with which he purports to deal is very thorough; the question of treatment is outside its scope and is not touched upon, except in so far as it enters into prophylaxis. We find no mention of blackwater fever, which is a pity for Professor Missiroli would probably be able to throw valuable light on the present obscurities of this condition; at least we would look for an admirable summarization of the present position of the problem.

The subject is dealt with in the following order:—a chapter on the history and distribution of malaria, first a general review and then a more detailed account of its prevalence in Italy in ancient and in modern times. A graph shows the fall in mortality from 1887 to 1930 and two maps indicate by the depths of shading the reduction in malaria and malarial cachexia in the triennia 1887-89 and 1928-30. The next chapter describes the epidemic types of the disease and their distribution and seasonal prevalence in Italy, and this is followed by a chapter on the various species of plasmodium and their life-histories, including those of birds, anthropoids, smaller mammals, reptiles, etc., the methods of staining, technique of cultivation and the study of them by inoculation methods. The sources and modes of infection are next dealt with; the species of *Anopheles*, types of eggs, the geographical distribution, the biological differences of the various strains or races of *A. maculipennis* and the relation between their dis-

tribution and malaria prevalence. The Missiroli-Hackett precipitation reaction here finds a place. Chapter VI is concerned with the survey of a malarious district and the mode of carrying it out, with dissection of mosquitoes, measurement of endemicity, splenic and parasitic indices, examination of blood and Henry's sero- and melano-flocculation and interpretation of results.

The final chapters are devoted to measures of prevention as they may be applied to man, to the mosquito and to the district—oiling, the use of Paris green, of larvicides, drainage, changing the degree of salinity of a breeding site, general bonification, etc. The choice of site, erection of houses and their protection in malarial zones, and an account of the organization of anti-malarial campaigns complete the work.

The whole is well illustrated with various graphs, plates and figures. There is a fairly full list of contents, but this cannot take the place of an index with which a work of this kind, a sort of encyclopaedia *in piccolo*, should certainly be provided. The book deserves to be, and doubtless will be, widely read.

H. H. S.

VAN NITSEN (R.) [Médecin en chef de l'Union Minière du Haut Katanga] & DUWEZ (J.). [Ex-Pharmacien Chef de Service aux Troupes Coloniales]. **Traitement et prophylaxie des maladies des pays chauds.**—380 pp. 1934. Bruxelles: Imprimerie des Travaux Publics, Société Anonyme, 169 rue de Flandre.

A book divided into two sections: the first (158 pages) as the authors say in their preface, is an attempt to give in condensed form therapeutic methods employed in the treatment of tropical diseases including those suggested in more modern literature; the second (200 pages) is a form of abridged Belgian pharmacopoeia.

The diseases dealt with are those commonly included under the term tropical diseases and they appear in this book in alphabetical order. The treatments advocated are essentially on the side of drug treatments and details in regard to the care of the patient are dismissed in a few words. To those who are ignorant of Belgian medicine the long lists of remedies which are here given place would perhaps cause dismay. Though perhaps in no branch of medicine is active treatment so often demanded, yet with this book in his hand it would be difficult for the younger practitioner to learn to appreciate the value, on occasion, of a little "masterly inactivity."

As an example it is proposed to cite here the preparations which are advised in the treatment of blackwater fever, in this order:—to arrest haemolysis—snake antiserum, hemostil, or other antiserum, calcium chloride, hypertonic saline, intravenous glucose and sodium bicarbonate: to maintain diuresis—soda and Vichy water, cupping, injections of mephrine, lactose, theobromine, urenil, salyrgan, neptan, cyanide of mercury, papaverine; also biocholine, colloidal iron and arsenic, adrenalin, transfusions, etc. Nowhere is the danger of syncope, if the patient sits up, mentioned. Prophylactic measures are dismissed in a few sentences. The book will doubtless be a useful one to medical men practising in Belgian and French colonies. It contains some useful information, and some points sometimes forgotten by our own medical officers but as a whole it will be quite useless in the hands of the British tropical practitioner.

H. S. Stannus.

PATERSON (A. R.) [Director of Medical Services, Kenya Colony] with the Assistance of Many Officers of the Agricultural, Education, Forestry and Medical Departments of Kenya. **The Book of Civilization. Part I. On Cleanliness and Health, the Care of Your Children, Food, and how to get rid of Flies.**—pp. xiii+80. With 14 figs., 6 plans & 2 coloured plates. 1934. London : New York : Toronto : Longmans, Green & Co. [1s. 6d.] [Review appears also in *Bulletin of Hygiene*.]

For some years workers in different parts of the tropics have been emphasizing the necessity for recognition of the divers factors which contribute to disease production. Scientific methods of preventive hygiene must be based nowadays on a study of many subjects, such as the diets of the people, their housing conditions and the bearings of custom and traditional belief on health. It is therefore interesting and encouraging that a director of medical services in an important tropical colony should undertake the preparation of a book such as the one under review. It is a sign that the wider outlook in regard to tropical disease problems is being accepted as essential for their ultimate solution.

This book is the first of a series of parts written or to be written, arranged as Dr. Paterson calls it, for Africans, and an extensive program of instruction for self-help in housing, farming, stock-raising and much that appertains to the economic life of natives is outlined. It is a type of book which will make demands for collaboration on the part of many non-medical people.

Part one deals with the causes of sickness and the necessity for cleanliness as to village and house, hands and skin, clothes, cooking pots, food and drinking water ; outhouses, gardens and fields are discussed ; a useful chapter on the care of very young children is included. Food and flies and the means of getting rid of the latter are considered in some detail.

The book is adorned with quaint and amusing illustrations which may well appeal to the native mind. It is not a book with which the medical man in the tropics will always find himself in agreement, in detail or even in some larger issues. For example, it may appear unlikely that the future development of native farmers and villagers will be along the lines which the author envisages for Kenya. To some the thought will occur that the lot of the woman under the suggested régime is likely to be extremely laborious and they may think that it would be better to teach a girl properly on domestic matters, rather than leave this education so largely to a not too well-informed husband. In England the old policy of three acres and a cow has not much appeal in these days of laid-on water supplies, and efficient systems of disposal of excreta and refuse. The tendency in all countries which are advancing seems to be rather in the direction of less and less individual responsibility for these basic matters of public health. The suggestion of the use of filters for drinking water will appear to many readers not only inadvisable, but fraught with danger.

Nevertheless this is a book which will stimulate thought ; and there are many practical hints and a great deal of sensible information in it. The instructed reader may discover little he does not already know, but he will often be struck by the novelty in the mode of presentation.

D. B. Blacklock.

KOLLE (W.) [Director, Inst. Experim. Therap. etc.] & HETSCH (H.) [Professor Inst. Experim. Therap., Frankfurt]. **Experimental Bacteriology in its Applications to the Diagnosis, Epidemiology, and Immunology of Infectious Diseases. Vol. 2.** [Edited by JOHN EYRE, M.D., M.S., etc.].—613 pp. With 62 plates & 120 text figs. 1934. London: George Allen & Unwin, Ltd. [30s.]

The treatise on experimental bacteriology by Kolle and Hetsch, the seventh edition of which appeared in Germany in 1929, has been translated into English under the editorship of Professor Eyre, who has in some respects introduced new matter, thus rendering the book less out of date than it would otherwise have been. There are two volumes which were published in September and December 1934 respectively, but it is with the second volume alone that we are dealing here. This volume, apart from seventy pages at the beginning devoted to tuberculosis and leprosy, concerns subjects which are not strictly bacteriological, namely spirochaetal and protozoal infections, and diseases due to filterable viruses and rickettsias, while there is a chapter at the end on filamentous fungi and yeasts. As the name of the book implies, it is with the experimental side of the subject that the book particularly deals, though brief accounts of symptomatology, pathology and treatment are given where these are well defined. The book is based on laboratory work and its results, and in it will be found descriptions of the various parasites themselves, the methods of their culture and identification, the procedures which are adopted for the detection of their presence in the human or animal body, the methods of their spread from one host to another, including insect transmission, the development of immunity both active and passive and the whole subject of animal inoculation and experiment. Such subjects as syphilis and relapsing fever; malaria, amoebic dysentery and trypanosomiasis; yellow fever, rabies, small pox and typhus; foot and mouth disease and rinderpest; are all discussed according to the above plan. The mention of these serves to indicate the general scope of the book which is fully illustrated with 118 plates, many of them coloured, and 200 text figures. Readers will find that the book gives them a good, solid foundation of knowledge, but they will be disappointed if they expect too much in the way of the very latest information. One is even led to suspect that this would have applied in many respects even to the German original five years ago. However, the book will undoubtedly be a very useful one to possess as a guide to the generally accepted knowledge of a subject up to a certain date. *C. M. Wenyon.*

CARTAÑA CASTELLA (Pablo) & GIL COLLADO (Juan). **Estudio de las ratas y de sus ectoparásitos en ocasión del brote epidémico de peste en Barcelona en 1931.** [Rats and their Ectoparasites with Regard to the Barcelona Outbreak of Plague in 1931.].—116 pp. With 7 figs. & 12 plates. 1934. Comision Permanente de Investigaciones Sanitarias. Direccion General de Sanidad. Madrid.

More than half of this well considered and clearly written work deals with the subject of plague in general and incidentally with the application of these generalities to conditions in Barcelona. The work is divided into eleven chapters the last of which gives a summary and conclusions.

The first chapter gives a classification of the "domestic" rats and a key for identification of the genera and species, together with a list of their synonyms. A second subdivision of this chapter speaks of diseases common to man and domestic animals and the relation of the latter to the former,

e.g., plague, pseudo-tuberculosis, tularaemia, sodoku, trichinosis, infective jaundice, typhus, etc. Chapter II deals with the ectoparasites of the rodents, their life-histories, with excellent photographs and a key to the fleas and the acarines. This is followed by three chapters treating in more detail the biology of rat-fleas, their seasonal prevalence, their anatomy and mode of transmitting plague. Plague infection of rats is the subject of Chapter VI, both natural and experimental infection; in the former, the acute and chronic forms and those in which there are no detectable macroscopic lesions; in the latter the results of the different routes of infection, cutaneous, subcutaneous, intraperitoneal, alimentary tract, etc.

The remaining chapters are devoted to conditions as found in Barcelona. The results of autopsies on Barcelona rats are detailed and depicted in good illustrations in Chapter VII. The succeeding chapter deals with bubonic plague in the town from 1905, with a spot map showing the distribution of human cases in plague years; 1905 with 52 cases and a fatality rate of 19.6 per cent. [? 10 cases]; 1919 [total number not stated, but at least 7]; 1920 a single case; 1922, 28 cases in October and November; 1923, two cases, one each in November and December; 1925, one only, in March, a man who brought a cargo of plantains from the Canary Islands; 1930, four cases in October, all fatal, and 1931, 31 cases in August-December 8 fatal. In Chapter IX this last outbreak is described more minutely, the course of the outbreak and clinical characters of the cases; there follows a discussion as to the source which was not determined, whether infected rats, or fleas, or merchandise or a human case. Reviewing all these outbreaks [those of 1920 and 1925 can hardly be called outbreaks, seeing that there was but a single case in each], September-November seemed to be the usual time of prevalence, but in the 1905 outbreak which continued from June of that year to the following April, there were 15 in July and 19 in January.

The usual methods were adopted for dealing with the outbreak—notification of suspected cases, examination by experts, removal of the patient and contacts to the Infectious Diseases Hospital and isolation of the former, bacteriological diagnosis for confirmation, destruction of rats, etc.

The penultimate chapter is an account of a study of the Barcelona refuse dumps and illustrations show how insanitary dwellings, mere shacks, are in close proximity. A discussion follows on the chief methods of dealing with the town refuse, whether by incineration or by fermentation processes and subsequent use for agricultural purposes.

In the final, summarizing chapter the authors state that 8,074 rats were examined both for themselves and for their ectoparasites and 4,268 bacteriologically. Over 99 per cent. of the rats caught were *E. norvegicus*. As regards their swimming powers, the authors' experiments showed that *E. norvegicus* cannot keep afloat, in fresh water at all events, for more than 5 minutes and drowns in that time; it makes no effort to swim after 3 minutes. Some authors have stated that it can swim half a mile and can traverse a river such as the Volga.

Of 4,992 fleas caught on the rats 1,985 were *X. cheopis* and 1,643 *C. fasciatus*, *i.e.*, 39.8 and 32.9 per cent. respectively. Of all the 4,268 rats examined bacteriologically between July 1931 and January 1934, only one (in September 1931, that is in the epidemic period) showed signs indicative of plague and came from a place where four human cases had occurred. Inoculation experiments from it into guineapigs nevertheless were negative.

The authors conclude that they do not believe there was any connexion between the outbreaks on epidemiological grounds, nor that since 1905 there has been a latent enzootic of the disease. They maintain that there is a definite connexion between rats, refuse dumps and plague and that prophylactic measures must include solution of the house refuse problem and systematic rat destruction.

H. H. S.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 5.]

RELAPSING FEVER: SOME RECENT ADVANCES.

By E. HINDLE, M.A., Sc.D., Ph.D.

Sectional Editor, Tropical Diseases Bulletin.

(Received March 1st, 1935).

The present article comprises references to some of the more important recent advances in our knowledge of human relapsing fevers. With few exceptions attention will be confined to papers that have appeared during the last five years, since the writer's article on blood spirochaetes (HINDLE, 1931), contains a brief summary of our knowledge of the subject up to 1930, based on publications previous to that date.

Epidemiology.

In recent times there has been a remarkable diminution in the number of cases of relapsing fever in Europe and North Africa, but in 1930, endemic foci still persisted in Italy and especially Russia (League of Nations Report, 1930). Contrasting with this post-war decline in European countries, an extensive and deadly epidemic of louse-borne relapsing fever swept across Equatorial Africa, starting from Upper Guinea about 1921. According to LASNET (1930) the disease was probably introduced by natives from the Mediterranean region, as the first cases at Kouroussa occurred among Moroccan and Algerian soldiers. It spread down the Niger and during 1922 epidemics occurred towards the east in the Dori region, and the number of deaths caused during the first two years in the French Sudan and Niger is estimated at 80,000 to 100,000. In 1924 it spread to the Upper Volta region and across to Koutiala, causing at least 20,000 deaths. In 1925, it broke out in the Lake Chad region and invaded Northern Nigeria and the Cameroons. It persisted until 1929 in North Equatorial Africa and about 10 per cent. of the population is estimated to have died of the disease, the mortality varying from 5 to 25 per cent. of the whole population. The epidemic reached Darfur in September 1926, and according to ATKEY (1929) in one district alone 10,000 died out of a total population of 45,000. It was brought under control in 1928, although subsequently isolated outbreaks have occurred from time to

time. Apart from this great epidemic, a number of smaller outbreaks have been recorded in other parts of the world, among the more interesting being sporadic cases of tick-transmitted relapsing fever in North America (see below).

The following list comprises a brief summary of publications during the past five years dealing with cases of relapsing fever arranged according to the countries in which they occurred.

Europe.—SYSSINE (1931) records a steady diminution of the disease in Russia, from 19,701 cases in 1925 to only 1,656 in 1930.

Asia.—SACHS (1934), in a detailed analysis of relapsing fever in Chitral during 1932 and 1933, considers that the clinical evidence supports the view that both tick and louse-borne varieties were present. TSCHIREJKIN (1930) describes 10 cases of Bokharan relapsing fever; KATZ (1930) gives an account of 38 cases of the "Persian variety" observed in the Western Pamirs, and KASSIRSKY (1933) a description of the main features of Central Asiatic tick fever based on a study of 78 cases at TASHKENT. ROBERTSON (1932) contributes a general discussion of relapsing fever in China, with special reference to Shanghai, where the clinical symptoms resemble those of the European strain. CHU, DEITRICK and CHUNG (1931) give the results of a study of 26 cases in children in Peking, and HIROKI (1933) isolated strains of Manchurian relapsing fever and studied them with special reference to the persistence of residual brain infections. TOYODA (1931) gives a general review of the subject with special reference to the Manchurian strain.

Africa.—Numerous papers have been published on the various strains of relapsing fever occurring in North Africa and their relation to the infections occurring in wild rodents. In Morocco, DELANOË (1929) considers that at least three strains may occur, *S. recurrentis*, the ordinary European form, *S. hispanica*, or a related form, causing the Spanish-African type of relapsing fever, and *S. marocana*, causing a mild non-relapsing type. On the other hand, NICOLLE and ANDERSON (1929b) find that all the strains of tick-transmitted relapsing fever in Morocco belong to the same species, *S. hispanica*. This Spanish-African strain, variously referred to as either *S. hispanica*, or *S. hispanica* var. *marocana*, has now been recorded from Algeria, by SERGENT (A.), MANCEAUX and BALLISTE (1933), and HORRENBERGER (1933). In Tunis, NICOLLE, ANDERSON and LE CHUITON (1931) observed three cases of the same strain, which were also studied by NICOLLE, ANDERSON and LAIGRET (1932) and two further cases by NICOLLE, LAIGRET and SICARD (1933). What seems to be a new strain of the *hispanica* group, has been isolated by ANDERSON and WASSILIEFF (1933) from *Ornithodoros erraticus* collected from burrows of *Meriones shawi* in South Tunisia. In Cyrenaica (Tripoli) cases of relapsing fever, probably tick-transmitted, have been recorded by FRANCHINI and TADDIA (1930) and MEDULLA (1931). A focal epidemic in Asmara, Eritrea, is supposed by DE PAOLI (1930) to have been introduced by travellers from Abyssinia.

Further South reference has already been made to the great epidemic of louse-borne relapsing fever which devastated North Equatorial Africa from 1921 to 1929, described by LASNET (1930), CAZANOVE (1930) and LE GAC (1931). Also a small epidemic occurred during 1927 and 1928 in villages of the Dori region (MALTZER, 1929). RUSSELL (1931), contributed a valuable study of cases occurring in the Gold Coast during 1929 and 1930.

Our knowledge of tick-transmitted relapsing fevers in West Africa, especially at Dakar, is summarized by MATHIS (1931). The discovery of *Ornithodoros erraticus* in that region by DURIEUX (1932) removed the problem surrounding the transmission of the local strain of *S. duttoni* (= *S. duttoni* var. *crocidurae*), for until then no one had succeeded in finding *Ornithodoros* in Senegal. MATHIS and DURIEUX (1934a) and FEYTE (1932) have brought forward evidence in support of the view that the disease is probably much more common in Dakar than the number of recorded cases would lead one to suppose.

ADVIER, ALAIN and RIOU (1934) have given a general account of cases observed in Dakar and other parts of Senegal, and call attention to the difficulties of diagnosis, as spirochaetes were found in the blood of only 25 out of 46 patients, and even then were extremely rare. MATHIS and DURIEUX (1934b) demonstrated the existence of an endemic centre at St. Louis, Senegal, whilst DUBOIS (1931a) compared two strains of *S. duttoni* from different parts of the Congo, and found that they were immunologically distinct.

America.—Although previously suspected, the first definite record of the existence of tick-transmitted relapsing fever in the U.S.A. has been made by WELLER and GRAHAM (1930), who traced cases of the infection in Central Texas to a cave in the Colorado River Valley, containing large numbers of *Ornithodoros turicata*, the transmitting agent. Subsequently sporadic cases have been recorded from various other parts of the Southern United States. PORTER, BECK and STEVENS (1932) give a useful summary of 30 cases in California, where there is good evidence that wild rodents harbour the infection. (See also LEGGE, 1933). In addition, PALMER and CRAWFORD (1933) give details of six cases occurring in British Columbia, the first record of relapsing fever in Canada, where the wood tick, *Dermacentor andersoni*, is considered to be the most probable vector.

Relapsing fever in California has been the subject of a detailed account by COLEMAN (1933 and 1934 a & b), based on the study of three strains isolated from human cases. These strains were found to differ from *S. duttoni* and *S. novyi*, as judged by cross-immunity tests. Relapsing fever in Texas has been studied by KEMP, MOURSUND and WRIGHT (1933), who found that it was immunologically identical with *S. novyi*. Subsequently (1934), these authors made transmission experiments with *Ornithodoros turicata*, comparing the Texas strain with four other strains, *S. novyi*, *S. kochi*, *S. duttoni* and *S. recurrentis*. In feeding experiments none of these four strains could be transferred from rat to rat by *O. turicata*, and the spirochaetes died out in the tick within a week of being ingested. BRUMPT (1933) on the basis of similar results, named the causative organism *Spirochaeta turicatae*, as it differs from *S. novyi* in being transmissible by *O. turicata*.

DUNN and CLARK (1933) give a general account of relapsing fever in Panama, where it is known to have been endemic since 1905. *Ornithodoros talaje* and *O. venezuelensis* are prevalent and both have been shown to be efficient carriers.

Animal Reservoirs.

Since NICOLLE and ANDERSON (1927) developed the interesting hypothesis that small mammals, and especially rodents, commonly serve as reservoirs of infection for relapsing fever, there has been abundant evidence in support of their view in the large number of wild rodents that have been found naturally infected with various strains of

spirochaetes, pathogenic to man. In addition, collections made from the burrows of rodents have often revealed the presence of infected ticks, which had previously escaped notice. As might have been expected, much of the work on this subject has been conducted by NICOLLE and his colleagues, working in North Africa, where strains of relapsing fever have been isolated from a number of animal sources.

DELANOË (1929) isolated a strain of Moroccan relapsing fever (*S. hispanica* var. *marocana*) from *Ornithodoros* collected from the burrows of porcupines in Morocco, and later (1930) from the porcupines themselves. The strain was pathogenic to guineapigs and three men inoculated with infected blood from these animals showed scanty spirochaetes from the 8th to the 10th day. NICOLLE, ANDERSON and COLAS-BELCOUR (1929) found that a young porcupine could be infected with this strain and its blood became infective to other animals, but in view of the comparative rarity of the porcupine and its habitat, it is not considered to be as likely a host as the common small rodents.

Algerian foxes have also been found naturally infected with the Moroccan strain (DELANOË, 1931a) and infected *Ornithodoros* have been collected from their burrows. Spontaneous infections with the same strain also occur in the jackal and hedgehog (DELANOË, 1931b). According to BLANC, NOURY and FISCHER (1933), another important reservoir of this strain is the common grey rat, *Mus norvegicus*, for at Casablanca at least 1 in 22 was infected, as tested by the inoculation of their brains into guineapigs. DELANOË (1933b) also found a young weasel, *Putorius vulgaris*, caught in Morocco, naturally infected with *S. hispanica*. The central nervous system of this animal remained infective after the blood had become negative. The examination of large numbers of wild animals in Morocco (DELANOË, 1931c), indicates that infection with this strain of relapsing fever is very widespread in nature and there is no likelihood of its being eradicated.

A strain isolated from Getulie squirrels (*Allantoxerus getulus*) by BLANC, NOURY, BALTAZARD and FISCHER (1933), is said to resemble the ordinary Spanish-African type; but DELANOË (1933a), in specimens collected at Agadir, found a blood spirochaete differing considerably from the typical *S. hispanica*, for guineapigs were refractory, as well as *Meriones*. Moreover, experimentally this worker failed to infect squirrels by subcutaneous inoculation of *S. hispanica*, and considers that it is not likely to be a reservoir.

ANDERSON and WASSILIEFF (1933) obtained a new strain of relapsing fever from *Ornithodoros erraticus* collected from the burrows of *Meriones shawi* in South Tunis. Porcupines inoculated with the strain had a short infection with visible spirochaetes; *Meriones*, a non-apparent infection, with no visible spirochaetes; and two human subjects had severe attacks, one of them being fatal.

A. SERGENT (1933) studying the locality of the first Algerian case of Spanish-African relapsing fever, found *Rhipicephalus sanguineus*, from the patient's dog, naturally infected with the spirochaete, as tested by the inoculation of these ticks into guineapigs. Moreover, this species was subsequently shown to be capable of transmitting the infection by its bite, so that Spanish-African relapsing fever can be spread not only by *Ornithodoros* but also by the dog tick.

Batches of ticks, *O. erraticus*, collected in or near Dakar from burrows of rats, were found by DURIEUX (1932) to be naturally infected with the local strain of relapsing fever, as tested by feeding experiments on 10

patients (MATHIS, DURIEUX and ADVIER, 1933, 1934). An examination of the local fauna by MATHIS and DURIEUX (1934a) shows that many of the rodents can serve as reservoirs of infection in addition to *Crocidura stamplii*, which is the most important. As tested by the inoculation of blood or brain emulsion into mice or rats, the following species were found to harbour the infection:—*Epimys decumanus*, *E. alexandrinus*, *E. rattus*, *E. golonda campanae*, *E. coucha*, and the common wild mice *Mus musculus gentilis* and *M. m. spretus*. The two latter, however, were only rarely infected. Similar experiments, also by MATHIS and DURIEUX (1934b), showed that wild rats, *Epimys decumanus* and *E. golonda campanae*, collected in St. Louis, Senegal, and the neighbourhood, were naturally infected with the same strain of relapsing fever. ADANT (1932) examined wild rodents from various parts of Katanga Province and found a wild rat, *Aethomys kaiseri*, infected with a strain of relapsing fever pathogenic to man, but not to guinea-pigs, thereby differing from the Spanish-African strain.

In California, PORTER, BECK and STEVENS (1932) obtained the infection from nine chipmunks and two squirrels, by the inoculation of their blood into white mice, and further support to the view that field rodents are victims of spirochaetes which may be conveyed to man, is afforded by the record of a case in Sierra County, where the patient, a medical entomologist, was infected by the contamination of a wound with the blood of a freshly killed tamarack squirrel, which was subsequently found to contain spirochaetes (LEGGE, 1933).

In Panama, an extraordinarily wide range of animals has been found to harbour spirochaetes which seem to be identical with the human infection, including marmoset monkeys (*Leontocebus geoffroyi*), opossums (*Didelphis marsupialis ctensis*), armadillos (*Dasybus novemcinctus fenestratus*), calves and a horse (DUNN and CLARK, 1933). It would seem, therefore, that in the case of tick-transmitted relapsing fevers, a wide range of animals may serve as reservoirs for the infection, and the importance of any species in this connexion probably depends to a large extent on its numbers and habitat, and especially on its proximity to human habitations. Consequently, the smaller rodents are likely to be the most important carriers.

Transmission.

In nature, all known varieties of relapsing fever are transmitted exclusively by the agency of lice, ticks, especially those belonging to the genus *Ornithodoros*, and possibly of bed-bugs. With reference to the latter, recent observations tend to show that the bed-bug is a more favourable host than was previously suspected, and although epidemiological evidence does not support the view that they are of any great importance as carriers, yet their possibilities cannot be entirely ignored. ROSENHOLZ (1927) in a careful series of experiments found that when spirochaetes were ingested by bugs the organisms invaded the haemocoel and persisted there indefinitely, although they gradually disappeared from the gut. These spirochaetes in the haemocoel retained their virulence and presumably could reproduce the infection in human beings in the same way as the body-lice, by the infected contents getting on to an excoriated surface, since the mere bite of these infected bed-bugs was quite innocuous. CZARKOWSKA and BLANK-WEISSBEG (1930) found that spirochaetes persisted in the gut of the bed-bug up to 46 days after an infective feed, but became motionless after 48 hours. Active spirochaetes appeared in the haemolymph after 6 to 7 days and

the injection of infected bugs up to the 15th day, and also of haemolymph, produced infection in mice. KLEINE and KRAUSE (1934) found that when larvae of bed-bugs were fed on mice infected with both European and African strains of relapsing fever, about 4 per cent. remained infective up to 80 days after the infective meal. On the other hand 150 adult bugs similarly fed gave uniformly negative results, and also 3,000 larvae reared from infected parents were inoculated into mice without producing any infection. It is concluded, therefore, that these insects can only play a very small part as carriers of relapsing fever, not to be compared with that of ticks or lice.

Many species of *Ornithodoros* have been found naturally infected with spirochaetes infective to man, and NICOLLE and ANDERSON (1929a, 1929c) give further experiments in support of their view that any species of *Ornithodoros* is capable of transmitting all strains of relapsing fever normally transmitted by ticks belonging to this genus. They insist, however, that it is necessary to feed the ticks on the infected animal during the nymphal stage in order to succeed. DELANOË (1931c) also gives two examples of unsuccessful attempts to infect adult *Ornithodoros erraticus* with the Moroccan strain of relapsing fever. These conclusions are opposed by KRITSCHESKI and DVOLAITSKAYA-BARISCHEWA (1931) who transmitted both *S. recurrentis* and *S. hispanica* (Berbera strain) by the bites of *Ornithodoros papillipes* infected only in the adult stage; also by KLEINE and KRAUSE (1932b), who found that adult *Ornithodoros moubata* when fed on mice infected with *S. duttoni* became infective.

The discovery of *Ornithodoros erraticus* in Senegal by DURIEUX (1932) considerably extends the range of this important North African carrier, which has repeatedly been found infected with various strains of relapsing fever, even when collected from the burrows of animals far removed from human habitations. Among localities from which ticks infected with *S. hispanica* have been found may be mentioned pigsties, the burrows of porcupines and fox-holes (DELANOË, 1929), as well as the burrows of small rodents. Moreover, in addition to *S. hispanica*, this species of tick has been shown to be the natural carrier of the following strains:—*S. normandi* (NICOLLE, ANDERSON and COLAS-BELCOUR, 1929); a strain found at Carthage related to the latter, but referred to as *S. erralici* (NICOLLE, ANDERSON and LAIGRET, 1932); another human strain isolated by ANDERSON and WASSILIEFF (1933) from ticks collected from burrows of *Meriones shawi* in South Tunis; whilst in Dakar it takes the place of *O. moubata* as the carrier of the local relapsing fever, the agent of which was previously named *S. crociduræ*, but is now considered identical with *S. duttoni* (MATHIS, DURIEUX and ADVIER, 1933). This species also transmits a group of spirochaetes found in small rodents, including *S. gondii*, which is very feebly pathogenic to guineapigs and rats, and does not infect man (NICOLLE and ANDERSON, 1930).

Ornithodoros papillipes.—Successful transmission experiments with this species, using the tick-borne Central Asiatic strain of relapsing fever (*S. persica*, *S. sogdiana*, or *S. usbekistanica*), have been recorded by MOSKWIN (1929), KRITSCHESKI and DVOLAITSKAYA-BARISCHEWA (1931), and PAVLOVSKIĖ (1932). The latter worker failed to transmit the disease by *Ornithodoros lahorensis* and considers that *O. papillipes* is the only proved vector in Central Asia.

Ornithodoros turicata.—This widely distributed species seems to be the most important carrier of tick-transmitted relapsing fever in the

U.S.A. WELLER and GRAHAM (1930) traced cases of relapsing fever in Texas to a cave containing large numbers of these ticks. BRUMPT (1933) found that the Texas strains were readily transmitted to mice, rats, and *Peromyscus* by the bites of *O. turicata*, but all attempts to transmit *S. hispanica*, *S. duttoni* and *S. venezuelensis*, and also *S. novyi* (BRUMPT, 1934a), gave negative results. On the other hand, NICOLLE, ANDERSON and LAIGRET (1932) recorded the experimental transmission of a strain of *S. hispanica* found in Tunis, by the bites of *O. turicata*. The infection was by bite from one nymphal stage to the next. KEMP, MOURSUND and WRIGHT (1934) also obtained similar results, and working with *S. novyi*, *S. kochi*, *S. duttoni* and *S. recurrentis*, found that none of these four strains could be transmitted from rat to rat by *O. turicata*; moreover, the spirochaetes died out in the tick within a week of being ingested. The Texas strain, however, was easily transmitted by its bite, rabbits, monkeys and rats being infected. Although they state that hereditary infection has been recorded, it is curious that these authors failed to infect rats by the inoculation of saline suspensions of eggs laid by infected ticks.

Ornithodoros venezuelensis has been shown capable of transmitting a spirochaete occurring naturally in the blood of squirrel monkeys, *Leontocebus*, caught in the Republic of Panama (CLARK, DUNN and BENAVIDES, 1931). One man was infected by the bites of nymphal and adult ticks fed on an infected monkey about five weeks previously. A batch of 60 larval ticks, reared from adults that had fed on an infected monkey, failed to produce any infection when allowed to bite a human volunteer.

Ornithodoros talaje, another carrier of human relapsing fever in Central America, has been found infesting opossums in Panama, of which 10 per cent. showed spirochaetes in their blood, transmissible to marmosets, rats and mice (DUNN and CLARK, 1933).

The possibility of ticks belonging to genera other than *Ornithodoros*, serving as carriers of human strains of relapsing fever is supported by the observations of A. SERGENT (1933), who in Algeria found specimens of *Rhipicephalus sanguineus* from a dog naturally infected with a strain of *S. hispanica*. Larvae of this dog tick were fed on infected guineapigs and after moulting the nymphs were allowed to gorge on four normal guineapigs. After 17 days interval, one of these animals became infected, with numerous spirochaetes in its blood. In addition, PALMER and CRAWFORD (1933), consider that the wood tick, *Dermacentor andersoni*, is the most probable vector of cases of relapsing fever occurring in the West Kootenay district of British Columbia. LEGGÉ (1933) found only *Ixodes* on Californian field rodents naturally infected with a strain of relapsing fever.

The problem of what happens to the spirochaete after being ingested by its transmitting host has been rendered still more uncertain by recent publications. KLEINE and KRAUSE (1932a) fed "clean" *Ornithodoros moubata* on a mouse infected with *S. duttoni* and found that spirochaetes, as such, persisted in the ticks for at least 33 days, and also remained infective. In some of the ticks, however, the spirochaetes died out. On the contrary, MOSKWIN (1929), working with "clean" *Ornithodoros papillipes* and a strain of Bokharan relapsing fever, found that within 12 days of being ingested, spirochaetes had completely disappeared from all parts of the tick. Yet these ticks were infective up to 170 days after the infective meal. This author traced all stages from the spirochaete in the alimentary canal to granular and cyst-like

forms in the Malpighian tubules, salivary glands and ovaries, and the inoculation of these organs into guineapigs in all cases produced infection. HATT (1929) by a study of sections of *Ornithodoros moubata* infected with *S. duttoni*, found that spirochaetes entered the cells of the tick and segmented into coccoid or bacillary forms, from which short spirochaetes subsequently developed. In this particular example the spirochaetes completely disappeared within 3 days of ingestion, but in the case of *S. hispanica* in *O. savignyi* the spirochaetes were still segmenting on the 5th day, had disappeared by the 9th day, and the coelomic fluid remained negative till the 25th day, when it became strongly positive, with all stages from short forms up to complete spirochaetes. Similar results were obtained with *O. savignyi* infected respectively with *S. duttoni* and *S. normandi*.

An entirely different life-cycle for *S. anserina*, the common fowl spirochaete, has been advanced by KNOWLES, GUPTA and BASU (1927). As a result of incessant division in the gut of the tick the spirochaetes are said to become about one-third the length of the ordinary blood forms, and extremely slender. These so-called "*tenue*" forms then invade the coelomic fluid and when there generally show a very fine terminal flagellum at each extremity. These forms are found in all parts of the body but accumulate especially in the salivary glands, where they develop into normal spirochaetes. Finally, MARCHOUX and CHORINE (1930) as a result of the examination of the blood of fowls bitten by infected *Argas*, concluded that there is an invisible infective stage of the spirochaete in the blood before the appearance of spiral forms.

Chemotherapy.

Relapsing fevers are generally treated by injections of salvarsan, or one of its derivatives, but all strains do not respond satisfactorily (e.g., DICKINSON, 1932; DE LA CAMARA, FERNANDEZ MARTINEZ, DE BUEN and JUAREZ, 1932), and many attempts have been made to find more efficient therapeutic agents.

The method of administration is of importance, for KATZ (1930), in cases of tick-transmitted relapsing fever in the Pamirs, found that irregular doses of neosalvarsan merely prolonged the apyretic period without any appreciable alleviation of the symptoms. This author recommends three injections:—0.3 gm. on the first day of the attack; 3–4 days later 0.45 gm.; and finally, after 5–6 days interval, 0.6 gm.

ROSKIN and LEVINSON (1930) found that exposure to ultraviolet rays greatly increased the therapeutic and sterilizing action of salvarsan in mice infected with *S. duttoni*; 35 out of 47 irradiated mice were cured by one injection of salvarsan, as compared with only one out of 41 controls not exposed to the action of the lamp. Raising the body temperature, by keeping animals at 40°C. for two hours before and after an injection of salvarsan, has been found to have a very marked effect on residual infections (LEBEDEWA and GALANOWA, 1932). A number of mice infected with *S. duttoni* were treated in this way and 17 days later tested for sterility; all were found to have been completely sterilized, whilst out of the same number of controls treated at ordinary temperatures, 60 per cent. showed residual brain infections. An analysis of the organs of "heated" and control mice, showed that the brains of the former contained 5 to 10 times as much arsenic as those of "unheated" mice that had received the same dose of salvarsan. MENK (1931) recommends the use of a mixture of neosalvarsan and solganal, a gold preparation, which, in mice infected with *S.*

duttoni, was found to be approximately four times as effective as either of the drugs by itself.

For the treatment of human cases of tick fever in Nyasaland, J. TODD (1930) recommends the use of intramuscular injections of sodium potassium bismuth tartrate; for adults 0.2 gm. of the drug dissolved in 2 cc. sterile water on two successive days. Apart from being less expensive, the drug is said to be much more effective than novarsenobenzol, since the temperature is brought down within 36 hours and relapses are almost unknown.

HÁSKÓ (1933) tested the effect of 15 trivalent and 5 pentavalent arsenic compounds on mice infected with *S. duttoni* and found only one (BR 34) to give results comparable with neosalvarsan. Antimony in the form of Stibosan H471, was found to be effective in the treatment of infections with Central Asiatic tick fever. Bismuth-yatren A has been used with success in the treatment of mice infected with *S. recurrentis* (KRITSCHESKI, 1930), and many gold preparations have been tested with more or less favourable results, especially in the treatment of residual brain infections, or strains resistant to arsenical compounds. Among the gold salts that have been recommended may be mentioned Sulpho-crisolo I.S.M. (CUBONI, 1929a); Allochrysine (HOWARD, 1929); Triphal (BASKIN, 1931); Solganal, or Solganal B (DUBOIS, 1931b); and various gold compounds, of which Solganal gave the best results (TODA, 1931).

The method of action of drugs in the treatment of spirochaetal infections has been studied by various authors, who disagree in their conclusions. MORETTI (1929) in the case of arsenical compounds, found that splenectomy, or blocking the reticulo-endothelial system, greatly reduced, if it did not entirely abrogate, the effect of the drug; hence the integrity of this system is considered to be essential for successful chemotherapy. HÁSKÓ (1932), as the result of experiments with *S. recurrentis* in mice, came to the conclusion that this infection has a transitory paralysing effect on the reticulo-endothelial system, and suggests that drugs are first absorbed by the spirochaetes, and subsequently deposited in the tissues together with them.

STERNBERG and PINES (1933) concluded that in the case of Stibosan the drug acted directly on the spirochaete and not through the tissues of the host.

An interesting new method of studying these problems has been introduced by SINGER and FISCHL (1934) and FISCHL, KOTRBA and SINGER (1934), who, by means of chemical analysis of the mineral content of the spirochaetes, determine the amount of arsenic or gold present in these organisms before and after treatment with organic arsenical or gold preparations. Their results suggest that the chemotherapeutic agents unite directly with the spirochaetes, but further *in vitro* experiments led SINGER, KOTRBA and FISCHL (1934) to the view that the action is a complex phenomenon comprising three phases:—(1) A physico-chemical adsorption of the substance by the pathogenic organism; (2) a change in this adsorbed substance owing to the vital activities of the cell, resulting in the formation of an actual poison; and (3) the completion of cure by the immune substances of the organism of the host. FELDT (1934) used the same method in a study of the action of chemotherapeutic substances in rats infected with three strains of relapsing fever and spirochaetes; one normal, another resistant against salvarsan, and the other against solganal. It was found that the resistant strains contained approximately the

same (never less) quantities of arsenic or gold as the normal strain, a result which supports the view that salvarsan and solganal do not act directly on the parasites. The action of these compounds is supposed to be through the natural defence mechanism of the animal body, and the resistance of spirochaetes to be dependent on their resistance to this defence function. This view is also supported by the results of KROÓ (1934), who found that, in spite of the favourable chemotherapeutic index of arsenobenzol in the treatment of fowl spirochaetosis, one-day old chicks inoculated with the maximum tolerated dose were not cured, for after a time spirochaetes reappeared in their blood.

A summary of previous work on *S. duttoni* is given by GRAY (1929) who found that his strain was markedly resistant to organic arsenicals; also a bismuth compound, "Bismostab," had little or no effect on the disease. CUBONI (1929a), using an arsenic resistant strain of *S. duttoni* in mice, found that the infection could be cured by Sulfo-crisolo I.S.M., a gold preparation. FELDT (1932) succeeded in producing strains of *S. recurrentis* resistant against salvarsan and solganal, respectively. The salvarsan-resistant strain, after passaging in normal mice for 10 weeks lost its resistance, but the solganal strain was still resistant after 19 months. Resistant strains of *S. pallida* were also produced. According to KRITSCHESKI and DEMIDOWA (1932), when salvarsan-resistant strains of *S. duttoni* in mice are exposed to the action of sodium thiosulphate (0.05 cc. of a 2.5 per cent. solution per gm. body weight), they become susceptible to the action of salvarsan, in contrast with the original strains which retain their resistance. The alteration is supposed to be the result of new chemoreceptors being formed on the spirochaetes by the action of the thiosulphate.

Two strains of Manchurian relapsing fever, one producing residual brain infections and the other not, were found by TODA (1931) to be identical in their resistance to neosalvarsan. ROTHERMUNDT (1932), also with WICHMANN (1932), as the result of testing the effect of a number of chemotherapeutic substances, including arsenic, antimony, bismuth and gold compounds, on mice infected with *S. duttoni*, came to the conclusion that the examination of the brain for spirochaetes as a criterion of the efficiency of any chemotherapeutic substance, and also the use of persistent brain infections for general chemotherapeutic experiments, are of little value.

General Pathology.

The changes in the spleen histology of 15 fatal cases of relapsing fever in the Gold Coast have been described by RUSSELL (1932), who also gives a useful historical survey of the subject. The most important and characteristic change was found to be the occurrence of miliary lesions, consisting of a zone of congestion and cell infiltration round the Malpighian bodies. BRUMPT (1934b) found that guineapigs infected with a Central Asiatic strain, transmitted by *O. papillipes*, often showed a large clot apparently arising from the anterior end of the spleen, and the peritoneum contained a quantity of non-coagulated blood. A study of the effects of three strains of relapsing fever spirochaetes in the eyes of rabbits is given by IGRSHEIMER and BODENHEIMER (1928), who found that the spirochaetes may persist in the cornea after their disappearance from other parts of the body.

Changes in the leucocyte formula in relapsing fever are recorded by MURATFT and LE GAC (1930), who studied cases at Wadai, Central

Africa. Although the number of polymorphonuclears and mononuclears did not alter appreciably, a more detailed examination showed that the number of lymphocytes diminished whilst the mononuclears increased, and the polymorphonuclears increased at the expense of the eosinophiles. In addition, the Arneth index was always deviated towards the left. CHU, DEITRICK and CHUNG (1931), in children infected with relapsing fever in China, found the leucocyte count of little value, but thrombocytopenia was constantly observed in the febrile attacks, the number of platelets falling below 100,000, returning after recovery to 200,000 to 300,000. No prolongation of the bleeding or coagulation time was noticed. An examination of the blood of guineapigs infected with *S. hispanica*, by VAN DEN BRANDEN, DUMONT and NELIS (1930), showed that the blood sugar content remained unaffected by the presence of this spirochaete. The urine of guineapigs infected with *S. hispanica* was found to contain the virus at the height of the infection in 2 out of 6 animals; also the aqueous humour, but the vitreous humour was always negative (REMLINGER and BAILLY, 1929b).

IMMUNITY.

The discovery of soluble specific substances in spirochaetes (HINDLE and Bruce WHITE, 1934), has introduced a new method for the study of spirochaetal immunity. The isolation of these substances in each case has been effected by solution of the spirochaete in 0.5 per cent. NaOH, followed by extraction with industrial alcohol, treatment of the filtrate with acetic acid, then refiltration, and further precipitation of the filtrate with acetone. By a process of differential precipitation an acetone-insoluble fraction was obtained free from protein, which is considered to be either a carbohydrate or a carbohydrate-containing substance. It reacted in high dilutions with homologous antisera, producing a zone of precipitation at the junction of the solution and antiserum. Since repeated injections of the substance into normal rabbits failed to produce any precipitating antibodies, it is considered to fall into the category of haptenes.

In relapsing fevers the study of immunity is complicated by the fact that the spirochaetes of successive attacks often differ in their serological characteristics. A detailed investigation into the types of spirochaetes found in experimental infections with Indian relapsing fever, by CUNNINGHAM, THEODORE and FRASER (1934), shows that although in successive febrile attacks there is a tendency for the alternation of two main types, in addition, other types may develop following the first attack, or the first relapse. RUSSELL (1933) using African pouched rats, *Cricetomys gambianus*, infected with a strain of relapsing fever isolated in Accra, showed that the relapse strain ("B") was serologically distinct from that of the first attack ("A"). In successive passages if a rat infected with type B relapsed, it produced spirochaetes of type A, and conversely. In addition, a third type appeared in one of the second relapses. This author emphasized the importance of discounting results obtained with first passage animals when isolating strains of the relapse type, since, in addition to inoculating spirochaetes of this type, one also inoculates immune bodies against spirochaetes of the first attack, and the passive immunity thereby induced is liable to influence the type with which the animal is expected to relapse. JAKIMOW (1929) found that in a case of a Berlin strain of

S. recurrentis, the relapse strain was distinct from the original strain in about 50 per cent. of the cases tested; whilst GRAY (1929), in animals infected with *S. duttoni*, was unable to find any immunological difference between the spirochaetes of successive relapses, and failed even to demonstrate the presence of antibodies.

The problem of immunity in spirochaetal diseases, whether dependent on residual infections, or on the development of immune bodies ("sterile immunity"), is discussed by ARISTOWSKY and WAINSTEIN (1929) who found that it was possible to produce immunity against *S. recurrentis*, by the inoculation of dead spirochaetes. Also RUSSELL (1933) immunized *C. gambianus* against a West African strain by the inoculation of dead spirochaetes combined with immune serum. On the other hand, KRANTZ (1932) produced only a comparatively transient immunity by the inoculation of living spirochaetes and immune serum, and found that the administration of immune serum at the crisis of the infection actually had a harmful effect. KROÓ (1934) found that after the inoculation of dead fowl spirochaetes into one-day old chicks no immunity developed, but adult birds similarly inoculated developed a well-marked resistance.

BELEZKI and UMANSKAJA (1929) consider that antibodies, spirochaetolysins, play the most important part in protection against spirochaetes, as evidenced by their gradual dissolution in the organs and blood. Phagocytosis, although it takes place, is said to be comparatively feeble and to play a very subordinate part in the disappearance of the organisms. This view is supported by KALAJEW (1931); also by KRITSCHIEWSKI and RUBINSTEIN (1931), who found that both splenectomy and blockage of the reticulo-endothelial system did not abolish acquired immunity to *S. duttoni*. In addition, VELU, BALOZET and ZOTTNER (1931b) found that splenectomy, either before or after infection with *S. hispanica*, had no effect on the course of the disease. LEVADITI, MARIE and LÉPINE (1931), like KALAJEW (1931), concluded that the production of immunity is under the control of the nervous system, since it does not develop if the nervous centres are affected functionally or anatomically by a local infection. On the other hand, PLAUT and GRABOW (1930), in detailed experiments with *S. duttoni*, found that the termination of each attack was not dependent on the production of antibodies, and the sudden death of the spirochaetes is regarded as due to factors which have not yet been explained. KROÓ (1934), in the case of fowl spirochaetosis, considers that the development of spirochaeticidal antibodies and obvious immunity are different factors which vary at different periods in the life of the fowl.

The blood of certain animals seems to possess spirochaeticidal properties against *S. duttoni*, for CUBONI (1929b) found that the fresh serum of cattle, sheep and goats invariably killed all spirochaetes within 1-2 hours at 37°C. This property disappeared when the serum was inactivated by heating.

NOHIRA (1929) tested the immunity of the offspring of mice infected with a Manchurian strain. His results indicated that the offspring are often resistant, owing to the passage of immune bodies through the placenta, and not to antenatal infection of the young themselves. On the contrary, in the case of guineapigs infected with *S. hispanica*, REMLINGER and BAILLY (1929d), found that the spirochaetes passed to their offspring at all stages of gestation, but the milk was not infective.

Residual Brain Infections.

The discovery that relapsing fever spirochaetes may persist in the brains of animals for considerable periods after apparent recovery, has proved a valuable aid in the study of natural reservoirs, for many animals whose blood was negative have been found to harbour the infection in the central nervous system, and the inoculation of brain tissue is now a routine procedure in any such investigations. The factors influencing the production of such residual infections, which are by no means invariable, have been the subject of much discussion. According to KRISCHIEWSKI and BRUSSIN (1931) the different races of relapsing fever spirochaetes show varying degrees of neurotropism and somatropism, the African strains in general being highly neurotropic, and the Russian (presumably louse-borne) strains highly somatropic and very little neurotropic. This view is opposed by KOLLE, PRIGGE and ROTHERMUNDT (1931) who consider that the persistence of spirochaetes in the central nervous system depends essentially on low virulence and feeble development of antibodies; and ROTHERMUNDT (1928) records experiments with a Russian strain, usually not producing residual brain infections, which after its virulence had been lowered in various ways acquired the property of producing persistent brain infections in mice. HIROKI (1932), in similar experiments with a Manchurian strain of relapsing fever, found that altering the virulence did not affect the number of residual brain infections, and later (1933) in a statistical analysis of the comparative mortality of the African strains, which often produce brain infections, and the Manchurian strains, which do not possess this property, showed that there was no significant difference between them. His results are entirely opposed to those recorded by PRIGGE and ROTHERMUNDT and support the view that spirochaetes persist in the brain by virtue of a specific neurotropic character.

Alterations in the percentages of residual brain infections produced in mice by strains of *S. duttoni* and *S. hispanica* respectively, have been recorded by ROTHERMUNDT (1932). A strain of *S. duttoni* which constantly produced brain infections in 1926, four years later produced only 30 per cent. infected, but after passage through a human subject the incidence rose to 55 per cent. Similar results were obtained with the *crociduræ* strain of *S. duttoni*, and also with *S. hispanica*, but in the opinion of the reviewer, the possibility of different strains of mice varying in their susceptibility to neurotropic infection has never been taken into calculation and makes it difficult to assess the value of these and other similar experiments. SAGEL (1930) studied four African strains, two of which produced brain infections in the mouse, whilst the other two did not. A strain of *S. duttoni* and a Moroccan strain were found to lose their serological distinction, and to have increased their virulence to man, as a result of brain passage. REMLINGER and BAILLY (1929b), using a strain of *S. hispanica*, found that when inoculated intracerebrally spirochaetes persisted in the brains of guinea-pigs, and also in various refractory animals such as the fowl, pigeon and tortoise. In the latter, the spirochaetes remained alive approximately the same length of time as infected blood kept in glass pipettes (about 45 days).

MATHIS and DURIEUX (1930) found that residual brain infections were a constant feature in mice inoculated with the Dakar (= *crociduræ*) strain of *S. duttoni*, and might persist up to 235 days after the original inoculation, and they recommend the use of brain emulsions

for inoculation instead of blood, in order to reduce the number of animal passages necessary for the maintenance of this strain in the laboratory (MATHIS and DURIEUX, 1931). It is necessary, however, to be sure that residual brain infections are a feature of the strain, for LAGRANGE (1931), using a strain of *S. duttoni* obtained from BRUMPT, found that only one out of 11 mice showed a brain infection, although the majority of rats similarly inoculated had residual infections, the brain of one animal being infective 242 days after the original inoculation.

In the case of Californian relapsing fever, COLEMAN (1934) found that infection of the brain in mice did not persist after the blood had ceased to be infective. CUBONI (1929a) demonstrated residual brain infections in young guineapigs infected with *S. duttoni* up to 44 days after the disappearance of spirochaetes from the circulation. *S. hispanica*, which more readily infects guineapigs, has been recovered from the brains up to 100 days after inoculation (PAMPANA, 1929).

The conditions affecting the production of these residual infections have been studied by VELU, BALOZET and ZOTTNER (1931b) using guineapigs infected with *S. hispanica*. No matter what method of inoculation was used the spleen became infective as quickly as the brain, and it was concluded that the spirochaetes persisted in the brain because of the weakness of the defence mechanism in that part of the body. Splenectomy before or after infection, was found to have no effect on the course of the disease, and neither splenectomy nor blockage of the reticular-endothelial system caused spirochaetes to reappear in the circulation of animals with residual infections. SEMZOVA (1931) claims that alcohol greatly increases the chance of residual brain infections, for when mice that had been given 0.3 cc. of 15 per cent. alcohol daily for varying periods, were injected with *S. duttoni*, 37.1 per cent. of the brains contained spirochaetes, as compared with only 19.4 per cent. in the case of normal mice similarly infected.

The form in which spirochaetes persist in the brain is still the subject of discussion, LEVADITI, ANDERSON, SELBIE and SCHOEN (1929 and 1930), and also REMLINGER and BAILLY (1929b), maintaining that there is an invisible stage, whilst BEUNDERS (1932) and BEUNDERS and VAN THIEL (1932), although admitting the possibility of such an ultra-microscopic stage, incline to the view that spirochaetes, as such, persist in the brain, but are generally so rare as to escape notice.

Mixed Infections.

It is well known that when a susceptible host is simultaneously inoculated with trypanosomes and spirochaetes, the course of the infection is often prolonged.

VASSILIADIS and JADIN (1930) found that when mice containing large numbers of *S. hispanica* in their blood were inoculated with *Trypanosoma rhodesiense*, the incubation period of this latter infection was slightly prolonged and the death of the animal a little delayed. The action of *S. duttoni* on *Tr. pecaui* was found to be much more marked, the incubation period being prolonged from 2 to 12 days. On the other hand, VELU, BALOZET and ZOTTNER (1931a) found that the simultaneous inoculation of *S. hispanica* and *Tr. maroccanum* had no effect on the development of either infection.

KAWAMURA (1931) made the interesting observation that even one strain of spirochaetes might influence the action of another strain in the same host. Thus in mice inoculated with strains of *S. duttoni* and *S. hispanica*, either simultaneously, or separately with an interval of 24-48 hours, the resulting mixed infection persisted longer than either of the infections alone. Both

strains were recovered from the brains of mice after the parasites had disappeared from the circulation. The simultaneous inoculation into mice of three strains of relapsing fever, *S. recurrentis*, *S. duttoni*, and *S. marocana*, is stated by RUBINSTEIN and KAPUSTO (1931) to have resulted in the appearance of a new race of spirochaetes, serologically distinct from the three original strains. The new race was not simply a mixture, for it was passed through mice immunized against each of the three original strains and retained its antigenic properties. It remained constant for six passages in mice, but on the seventh passage the three original strains reappeared. It is difficult to accept these remarkable observations without independent confirmation, for strains of spirochaetes, especially those producing residual brain infections, are very liable to become mixed in the laboratory, as shown by NICOLLE and ANDERSON (1929d).

KAWAMURA (1931) also studied the effect of two strains of spirochaetes, *S. duttoni* and *S. hispanica*, on mice infected with *Trypanosoma brucei*. When inoculated simultaneously the duration of life of the infected animals was about 22 days, as compared with only 4 days when the spirochaetes were inoculated 2 days after the trypanosomes. Also, in mixed infections, the removal of the spirochaetes by a dose of solganal, resulted in the mice dying of trypanosomiasis within 6 to 7 days, whilst untreated mice lived 24 to 25 days. The spirochaete is supposed to act by strengthening the natural resistance of the organism, but in mice which had been "blockaded" or splenectomized, it produced the same effects as in normal mice.

Similar results are recorded by GRILLO and KRUMEICH (1934) in the case of guineapigs infected with either *S. usbekistanica* (= *persica*) or *Spirillum minus*, and *Trypanosoma brucei*. In addition, the life of guineapigs infected with *T. brucei* was prolonged by the injection of chemical substances, which raised the body temperature, or which produced alterations in the general metabolism. These authors are of the opinion, therefore, that in mixed infections the effect of the secondary infection is to give an additional stimulus to the defence mechanism of the host.

Therapeutic Uses.

Certain authors recommend the use of relapsing fever, instead of malaria, for therapeutic purposes.

Owing to the mildness of the fever, the invariable spontaneous cure, and the ease of inoculation, MÁS DE AYALA (1931) regards *S. hispanica* as the most satisfactory agent, and gives details of a clinical study of 230 cases. Direct vein-to-vein inoculation of 2-3 cc. of blood during a febrile attack is said to give the best results. REMLINGER and BAILLY (1929c) call attention to the advantages of this strain, for it can easily be maintained in guineapigs. The virus can be transported either by means of infected ticks, or by simply defibrinating infected blood and preserving it in glass pipettes plugged with cotton wool. Such blood was found to remain virulent for at least 20 days at room temperature (REMLINGER and BAILLY, 1930a).

Cultivation.

A simple new culture medium made from egg, which does not require the addition of serum, has been described by Li YUAN-PO (1933), who maintained strains of *S. recurrentis* in this medium for at least 38 generations without the cultures losing their virulence for mice.

SCHARRER (1934) found that this medium gave good results with the fowl spirochaete, equal to any of the ordinary media containing serum. MANTEUFEL and DRESSLER (1933) also obtained excellent results with this method, but in addition describe a new medium, consisting of pieces of allantoic membrane in Tyrode's solution, in which strains of *S. hispanica* remained virulent for at least 38 passages. On the other

hand, CONSTANTINESCO (1931), using a strain of *S. duttoni*, found that when cultured in plasma containing pieces of fowl embryo, or mouse brain and spleen, the spirochaetes rapidly lost their virulence.

MARCHOUX and CHORINE (1933), using a slight modification of Galloway's method, claim to have obtained cultures of an invisible but virulent phase of the fowl spirochaete. Cultures were obtained both from the blood and organs of infected fowls and also from infected ticks. The necessary anaerobic conditions were sometimes obtained by adding *Bacillus eucarians* to the medium, and mixed cultures of this nature, continued for at least 62 passages, still remained virulent.

LAUDAUER (1931) made further simplifications in this medium and studied the factors influencing the growth of the spirochaetes. JAHNEL (1933), using fowl spirochaetes grown in a serum medium, found that their virulence fell lower and lower with successive passages, especially if the cultures were grown at 37° to 40°C. After 43 subcultures the 4-day old cultures were still virulent, but 8, 12, 13 and 16 day-old cultures were all non-pathogenic. In earlier passages the virulence could be restored, but ultimately the spirochaetes lost their pathogenicity, although the ordinary growth and motility was unaffected.

Using four strains of relapsing fever grown in a simple medium of inactivated horse or rabbit serum diluted with saline, MORODER MUEDRA (1929) also found that cultures of spirochaetes might become completely negative to microscopical examination but retain their virulence. Very often these seemingly negative cultures showed small granules, resembling micrococci, but these organisms failed to grow on agar slopes. Out of 17 mice inoculated with cultures showing no trace of spirochaetes, 15 became infected with spirochaetosis after 2 to 4 days.

EBERSON and MOSSMAN (1931), for *S. hispanica*, recommend the use of hormone broth containing brain mash, or of a sodium-citrate dextrose medium containing brain tissue. Cultures were found to remain virulent for 2 months at 38°C. A life-cycle is stated to occur in the cultures, passing from a granular stage to the adult spirochaetal form, and the preparation of a cinematograph record of this evolution is said to be in progress.

SEGUIN (1930), in cultures of *S. calligyra* from genital condylomata, observed very small spirochaetes 1 to 2 μ long, each with a drawn-out extremity resembling a flagellum. These forms appear as mere granules under dark-ground illumination. All intermediate stages were found between these minute forms and the ordinary spirochaetes.

HINDLE and ELFORD (1933) have shown that spirochaetes, including *S. pallida*, pass readily through graded collodion filters, and this method furnishes a simple and effective means of separating them from other organisms and also of estimating their diameters.

Staining Methods.

To facilitate search for spirochaetes in blood PAMPANA (1931) recommends the following solution which keeps for months:—Methylene blue (B extra) 2 gm.; distilled water 100 cc.; dissolve, filter, and add 4 cc. of formalin and 10 cc. of glacial acetic. The blood is obtained in thick drops, and dried rapidly by holding over the microscope lamp. The stain is poured on and allowed to act for 10 minutes, then rapidly washed in running water, blotted and dried. The spirochaetes and nuclei of the leucocytes stain blue, and stand out amid unstained surroundings. WEISS (1929) finds that mordant methods give good results, since spirochaetes have a greater affinity for acid dyes, whilst bacteria usually take basic dyes. He recommends that the material containing spirochaetes be placed

on a slide in a drop of 5 per cent. glacial acetic acid, and then put in the incubator for 15 minutes, evaporation being prevented by covering with a hollow ground slide. The drop is then spread out on the slide and allowed to dry. The slide is then covered with a mordant prepared by mixing one part of a solution of 100 gm. tannic acid in 100 cc. of 95 per cent. alcohol, with two parts of undiluted formalin containing 7.5 per cent. acetic acid. After 2-5 minutes the excess mordant is washed off with warm water, and the film stained with a mixture of acid and basic dyes, such as gentian violet and acid green; brilliant green with acid violet, or with acid fuchsin, etc. The slides are stained for 2-5 minutes in a saturated solution of the basic dye, then washed off with water and covered for 10-30 minutes with the acid dye in 30 per cent. alcohol. The slides are finally washed in water, and allowed to dry without heating.

Du (1931) recommends the use of carbol fuchsin for one minute, after dehaemoglobinizing for 5 seconds with 6 per cent. acetic acid in 95 per cent. alcohol. After trying eight different methods VAN DEN BERGHE (1931) found the following to give the best results:—

Fix the film for 2-4 minutes in Ruge's formol acetic, or in alcohol containing 10 per cent. formalin; allow to dry, and stain for 2-3 minutes in a 3 per cent. aqueous solution of Victoria Blue 4 R (Grübler). Wash off the stain in water, and allow to dry.

General.

The necessity for the identification and control of relapsing fever spirochaetes maintained in laboratories is emphasized by NICOLLE and ANDERSON (1929d), who mention some examples of errors in the identification of well-known strains. They consider that the relapsing fever spirochaetes seem to fall into two groups: a very homogeneous *S. duttoni* group, all the strains of which are serologically identical, in marked contrast with the remaining forms, all of which show great variation and a tendency to break up into serologically different races, so that one could almost form new species out of each strain. The authors' views as to the specific identity of the strains of relapsing fever occurring in Spain and North Africa, have been criticized by DELANOË on the grounds that too large doses of spirochaetes were used in their cross-immunity tests. Accordingly, NICOLLE and ANDERSON (1932) repeated the tests with four races isolated from cases of Spanish-African relapsing fever, using different doses and methods of infection, and showed that the dosage is of no significance, and the races of spirochaetes isolated from different individuals showing the same type of disease can all be distinguished by cross-immunity tests, as well as by agglutination or lysis.

Many species of mammals have been shown to be susceptible to infection with various strains of spirochaetes. (See above "animal reservoirs"). REMLINGER and BAILLY (1929a) in the case of *S. hispanica* found that in addition to the invariable susceptibility of the guinea pig, the hedgehog, wild rats and wild mice could be readily infected, also with difficulty rabbits, young dogs and in one case a 3 months' old kitten. Adult cats were refractory, also the fowl, pigeon, martin, tortoise, frog and fishes. BODECHTEL (1930) found that *S. recurrentis* and *S. anserina* might be found in the blood of lizards, frogs and goldfish inoculated with these spirochaetes, but the organisms merely persisted for a few days and there was no evidence of multiplication.

The susceptibility of spirochaetes to the action of various cytolytic agents *in vitro*, is well shown by the action of sodium ricinolate which has been found by VIOLE (1934) to kill spirochaetes, even in dilutions

of 1 : 1,000 in media containing proteids. The exposure of *S. duttoni* to the total rays from a mercury lamp of 500 watts at 40 cms. for 18 to 30 minutes is said by LEVADITI, VAISMAN and PAFC (1934) to destroy the reproductive capacity without affecting the motility of these organisms.

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 — VAISMAN, A. & PAIC, M. (1934), **32**, 298.
- MALTZER, M. (1929), **27**, 691.
 MANTEUFEL, P. & DRESSLER, I. (1933), **31**, 92.
 MARCHOUX, E. & CHORINE, V. (1930), **27**, 701.
 — — (1933), **31**, 89.
 MÁS DE AYALA, Isidro (1931), **29**, 206.
 MATHIS, C. (1931), **29**, 206.
 — & DURIEUX, C. (1930), **28**, 303.
 — — (1931), **28**, 735.
 — — (1934a), **31**, 505
 — — (1934b), **31**, 849
 — — & ADVIER, M. (1933), **31**, 87.
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 MORETTI, P. (1929), **27**, 113.
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 MURATET, L. & LE GAC, P. (1930), **28**, 304.
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 — — (1929a), **26**, 658.
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 — — (1929c), **27**, 109.
 — — (1929d), **27**, 693.
 — — (1930), **28**, 731.
 — — (1932), **29**, 556.
 — & COLAS-BELCOUR, J. (1929), **27**, 107.
 — — (1929), **27**, 692.
 — & LAIGRET, J. (1932), **30**, 10.
 — & LE CHUITON, F. (1931), **28**, 731.
 — LAIGRET, J. & SICARD, M. (1933), **30**, 721.
 NOHIRA, A. (1929), **27**, 114.
- PALMER, J. H. & CRAWFORD, D. J. M. (1933), **30**, 721.
- PAMPANA, E. (1929), **27**, 696.
 — (1931), **28**, 737.
 DE PAOLI, P. (1930), **28**, 298.
 PAVLOVSKIĖ, E. N. (1932), **30**, 722.
 PLAUT, F. & GRABOW, C. (1930), **28**, 301.
 PORTER, G. S., BECK, D. & STEVENS, I. M. (1932), **30**, 361.
- REMLINGER, P. & BAILLY, J. (1929a), **27**, 107.
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 ROBERTSON, R. C. (1932), **30**, 360.
 ROSENHOLZ, H. P. (1927), **24**, 685.
 ROSKIN, G. & LEVINSON, L. B. (1930), **27**, 694.
 ROTHERMUNDT, M. (1928), **27**, 111.
 — (1932), **30**, 13.
 — & WICHMANN, F. W. (1932), **30**, 362.
 RUBINSTEIN, P. L. & KAPUSTO, M. L. (1931), **29**, 210.
 RUSSELL, Helen (1931), **28**, 730.
 — (1932), **30**, 362.
 — (1933), **30**, 363.
- SACHS, Albert (1934), **32**, 296.
 SAGEL, W. (1930), **28**, 300.
 SCHARRE, B. (1934), **31**, 853.
 SEGUIN, P. (1930), **27**, 700.
 SEMZOVA, O. M. (1931), **28**, 735.
 SERGENT, A. (1933), **31**, 88.
 — MANCEAUX, A. & BALLISTE, R. (1933), **31**, 87.
 SINGER, E. & FISCHL, V. (1934), **31**, 510.
 — KOFERBA, J. & FISCHL, V. (1934), **31**, 851.
 STERNBERG, E. J. & PINES, A. I. (1933), **30**, 723.
 SYSSINE, A. (1931), **29**, 555.
- TODA, T. (1931), **29**, 563.
 TODD, J. (1930), **27**, 694.
 TOYODA, H. (1931), **28**, 738.
 TSCHIREJKIN, W. Ch. (1930), **27**, 695.
- VAN DEN BERGHE, L. (1931), **29**, 564.
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 VELU, H., BALOZET, L. & ZOTTNER, G. (1931a), **28**, 734.
 — — (1931b), **28**, 736.
 VIOLLE, H. (1934), **31**, 852.
- WEISS, E. (1929), **27**, 115.
 WELLER, B. & GRAHAM, G. M. (1930), **28**, 299.
- YUAN-PO, Li (1933), **30**, 366.

LEPROSY.

LEPROSY REVIEW. 1934. Oct. Vol. 5. No. 4. pp. 149-197. With 15 figs. on 4 plates & 1 text fig. Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W.1. [2s.]

The most important paper in this issue is by F. G. ROSE on the curability of leprosy, based on many years work in charge of a campaign against the disease on modern lines in British Guiana, with the aid of a leper hospital and dispensaries for out-patient treatment of early cases found by surveys. Still more important, he has been able to follow up for long periods nearly all the discharged patients in a manner not yet possible in other leprosy countries, and to prove that not more than 14.1 per cent. have shown lasting relapses. Tables of the data are given and Dr. ROSE's own summary as follows speaks for itself.

"1. Of 801 patients suffering from leprosy under observation in British Guiana from 1926 to 1934, 138 have died, and 16 have left the country.

"2. Of the remaining 647, 180 are cases spontaneously arrested, leaving 467 who have undergone active treatment during this period.

"3. Eighty-six of these received treatment for less than a year, leaving 381 whose ultimate fate is considered.

"4. Two hundred and fifty-seven were early cases, of whom 76 are now arrested, 66 quiescent, and 66 improved.

"5. One hundred and twenty-four were advanced cases, of whom 22 are arrested, 15 quiescent, and 66 improved.

"6. It is suggested that arrested and quiescent cases in whom function has been completely restored should be termed recovered in addition.

"7. Of the 142 early quiescent and arrested cases, 100, and of the 37 advanced cases 10, have completely recovered.

"8. Ninety-eight cases have become arrested, of whom 13 have eluded observation.

"9. Of these 85, 14.1 per cent. have relapsed and have not yet become re-arrested.

"10. Relapse generally occurs within the first two years after the arrested stage has been reached.

"11. Treatment should be continued for at least six years after arrest.

"12. An arrested case may be deemed cured after six consecutive years of inactivity.

"13. Special attention should be devoted to childhood infection."

The Editor of the review has adopted the unusual procedure of asking leprosy experts, working under totally different conditions in far distant countries, to criticize Dr. ROSE's paper. The most experienced of these is Dr. E. MUIR of Calcutta, who strongly supports Dr. ROSE in the following findings among others.

" (2) The table of results in early cases corresponds to the results that we obtain in India in places where the patients attend regularly and are efficiently treated. (3) The results in advanced cases also correspond closely with results obtained in India under favourable circumstances." [The reviewer declined an invitation to comment on Dr. ROSE's paper as he accepts unreservedly the records and conclusions of that able and experienced worker.]

The evaluation of the results of treatment in incipient leprosy is once more dealt with by J. RODRIGUEZ, who repeats his experience that chaulmoogra preparations are less effective in the very early and often bacteria-free stages than in those with more developed dermal lesions containing abundant lepra bacilli. [This may possibly be due to the fact that destruction of the bacilli leading to a gradual production of immunity is an important factor in recovery.]

In a further yearly review of his leprosy work in Korea R. M. WILSON records the value of localized anaesthesia and nerve thickening in early diagnosis. In treatment he still finds injections of 5 to 7 cc. doses of pure freshly obtained hydnocarpus oil the cheapest, most satisfactory and most painless method. In 70 to 80 per cent. of early cases marked improvement is obtained. He has noticed a pellagroid condition of cases in the spring, and that most of the Korea cases come from the southern humid half of the country. A paper on dye treatment is dealt with below under that heading.

L. Rogers.

MARCHOUX (E.). La lutte contre la lèpre dans les colonies françaises. [**Anti-Leprosy Measures in the French Colonies.**]*—Internat. Jl. Leprosy.* Manila 1934. Aug.-Oct. Vol. 2. No. 3. pp. 311-314.

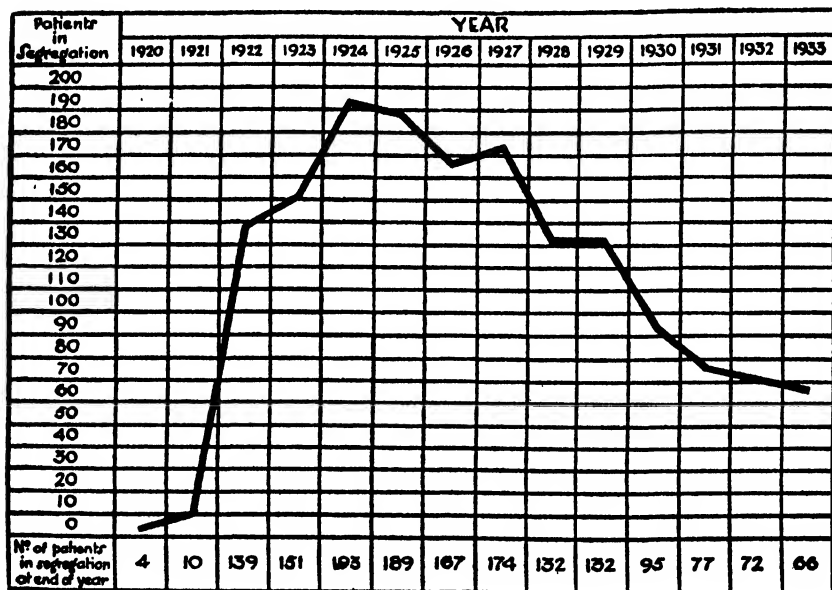
"The antileprosy campaign that has long been carried on in the French colonies, based on the internment of cases, has not given the expected results. The conditions of the measures in force, and a widespread idea that the disease is hereditary, have resulted in an attitude strongly antagonistic to the system in spite of efforts to ameliorate the circumstances of those affected, and the disease has not only persisted but is continually spreading. To deal with the situation the Minister of Colonies has appointed a permanent commission, composed of Drs. Marchoux, Jeanselme, Gougerot and Burnet, which has considered a revision of measures for leprosy control for the colonies.

"The principles approved are, briefly, that the disease is a communicable one, the germ of which escapes from the tissues only when there are ulcers, in the absence of which even prolonged contact is not dangerous; ulcers of the mucosa present a greater difficulty than those of the skin, and ulcers may be precocious and inconstant. Diagnosis should, therefore, be made as early as possible; this requires a skilled specialist, but an educated populace will make diagnoses by themselves, so there is need of instruction of the public in regard to this, and also regarding the dangers of contagion and the value of early treatment. The first task is to enumerate the cases and to classify them—cutaneo-mucous, nervous and latent being the three types enumerated. Methods of providing treatment under different conditions the desiderata as regards hospitalization, and the practicable methods of educational propaganda are enumerated."

L. R.

GRANT (Alan M. B.). **Leprosy at Nauru since 1928.**—*Internat. Jl. Leprosy*. Manila. 1934. Aug.-Oct. Vol. 2. No. 3. pp. 305-310. With 1 text fig.

This important article reports the further progress of the effort to reduce the high incidence of leprosy at Nauru by modern methods since the publication of Dr. BRAY's article in 1930 [see this *Bulletin*, Vol. 27, p. 997], which is conveniently reprinted in this issue of the journal. The 2,500 inhabitants are examined frequently for early cases of leprosy and only the infectious ones are segregated in accordance with the advice of L. ROGERS. The accompanying chart and table show that the infectious bacteriologically-positive cases have fallen from 193 in 1924 to 66 at the end of 1933, or by almost two-thirds within one decade, but the rate of decline is now less, partly owing to the admission of 16 cases without bacteriological examination in 1932. In addition 155 uninfected cases are attending clinics as out-patients, and none of these are discharged as apparently cured until after five years treatment with two years' freedom from all active symptoms; they live in separate houses and apart from any children. *Hydnocarpus* esters are used in treatment. In the last five years 83 have been paroled, and only 22 have relapsed, but 21 of 48 of discharged clinical cases were again given treatment for relapse. Nine have died in five years. Infants born in the isolation station are separated from their parents at birth. The author concludes that leprosy is slowly decreasing, that early diagnosis by frequent inspections has been of paramount importance, and that "the division of the cases into infectious and uninfected and the different treatment of these groups has given better results than would have resulted with compulsory segregation of every case of leprosy."



Graph showing the total number of cases of leprosy in segregation at the end of each year since the appearance of the disease at Nauru.

[Reproduced from the *International Journal of Leprosy*.]

Admissions, discharges and relapses at both clinic and isolation station, Nauru, during the five years, 1929-1933, inclusive.

Occurrence.	Year.				
	1929	1930	1931	1932	1933
Admissions, new patients to station ...	5	4	4	16 ^a	4
" " clinic ...	29	60	31	43	8
Discharges, patients from station ...	4	39	19	21	—
" " clinic ...	6	2	3	22	15
Relapses, admitted to station ...	—	—	—	—	11 ^b
" " " clinic ...	—	—	—	—	21 ^b
Total number of cases in station ...	132	95	77	72	66

a This number was admitted without bacteriological examination.

b Total for the five-year period.

L. R.

GOMES (J. M.). A lepra no Estado de S. Paulo. (Notas endemiológicas.) [**Leprosy in the State of S. Paulo.**]*—Mem. Inst. Oswaldo Cruz.* 1934. July. Vol. 28. No. 3. pp. 317-387. With 7 plates (2 maps). English summary pp. 388-390.

Leprosy has increased gradually in S. Paulo State during the last century with more active foci in certain areas requiring most attention. The great majority of these are found on non-sandy soil with high humidity. Examination of lymphatic glands and allergic manifestations indicate that a large number of contacts with open lepers become infected without showing signs of the disease, mostly during childhood, and more from their mothers than from their fathers. *L. R.*

DENNEY (O. E.). **The National Leprosarium, Carville, La. Review of the More Important Activities during the Fiscal Year ended June 30, 1934.**—*Public Health Rep.* 1934. Nov. 16. Vol. 49. No. 46. pp. 1359-1365.

In spite of a reduced budget the activities have been maintained at this institution. New admissions numbered 64, and 20 were paroled leaving 361. Chaulmoogra oil orally in from 3 to 155 drops three times a day was used in 225 cases, and benzocaine-chaulmoogra oil intramuscularly twice weekly in 123, while 50 were on esters intramuscularly. Several dyes were tried "without encouraging results." The usual special services were maintained. Initial apparent increase in acid-fast bacilli from leprous lesions was obtained on a variety of culture media, possibly due merely to concentration through autolysis of the tissues inoculated with them, but no active subcultures could be obtained.

L. R.

SHARP (Leonard). Further Report on Bunyoni Leper Colony, Kigezi, for 1933-34 with Statistics.—*East African Med. Jl.* 1934. Nov. Vol. 11. No. 8. pp. 245-255.

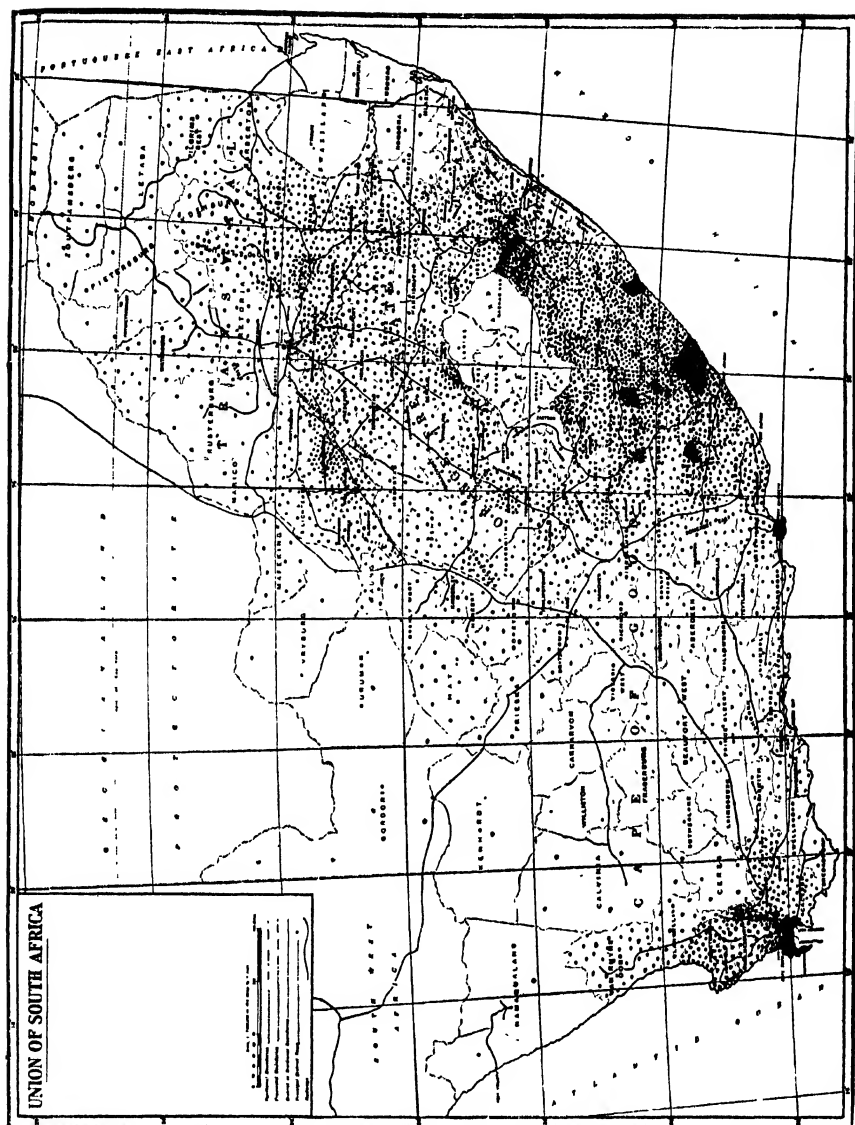
During a further year's work at this West Uganda island settlement the numbers under care increased from 300 to 522. Improved buildings and additional land for cultivation have been supplied and plantations of eucalyptus trees made. Over 100 children are being taught and 33

have shown arrest of the disease. A much needed home for untainted children has been built, for 57 per cent. of the children of lepers have become infected, and without separation from their parents probably 75 per cent. would eventually develop the disease. One-third of all the lepers in the colony are children under 15 years of age, 75 per cent. of whom are early or mild cases, and among 194 early nerve or cutaneous cases 43 per cent. have become arrested during the year and they constitute 92 per cent. of the total arrested cases. Similar tables to those of the previous year's report are given with 46 per cent. improved in addition to the 23 per cent. arrested, including all treated for three months or over. They are subdivided into numerous tables, three with only 2 to 5 cases and nine more with less than 20 cases, but the general conclusion come to is that those with no drug treatment did best and those with most injections did worst, brilliant green being better than chaulmoogra oil preparations. In view of the shortness of the treatment in some at least the results of the five years' treatment, found by Dr. ROSE to be necessary to obtain the best results with chaulmoogra preparations, will be awaited with interest. *L. R.*

UNION OF SOUTH AFRICA. ANNUAL REPORT OF THE DEPARTMENT OF PUBLIC HEALTH YEAR ENDED 30TH JUNE, 1934. [*Leprosy* pp. 31-45. With 6 maps (1 folding).]

This report is by Sir E. N. THORNTON and it takes a more hopeful view than earlier ones. The expenditure has fallen from £204,000 fourteen years ago to £154,000 when the health department took over the work in April 1924 and to £97,428 in the last financial year, which is still nearly one-fourth of the cost of the whole public health work. After some historical data and information for the enlightenment of the public on the low infectivity and chronicity of the disease, it is stated that : " In its early stages the disease is most amenable to treatment. Chaulmoogra oil still holds the field." The disease is decreasing among Europeans and there are probably fewer cases than once thought among non-Europeans. Tables show 2,155 total, but only 95 pure Europeans, segregated in leper institutions, which have now all been converted into well staffed hospitals. In addition there are 1 certified and 6 home segregated Europeans, 1,542 in all discharged probationally, but still under surveillance, and 889 released from surveillance as no longer requiring to be watched. Treatment remains voluntary and the ethyl esters and sodium salts of the lower melting point fatty acids are the most popular preparations. Compulsory segregation is still considered the only sound method in S. Africa.

An instructive study of leprosy incidence among non-Europeans from 1900 to 1930 has been made by Dr. J. F. WOOD and is illustrated by maps. The data show a rate of 1.9 per mille, 855 cases, in the Orange Free State, mostly the Northern and Middle districts. From the Transvaal there were 2,860 admissions, or 2.4 per mille, with most on the border of the Vaal River. Natal showed 1,424 cases, or 1.2 per mille, mostly along the Basutoland border. The Cape Province had 2,488 cases, or 1.5 per mille. The four smaller native areas show rates of from 2.6 to 3.7 per mille. A spot map of all the cases shows a remarkable concentration of cases in the eastern areas, especially around the hilly Basutoland, and in a small one near Cape Town. [The distribution of high rainfall is similar.] *L. R.*



Relative incidence of leprosy in non-European population of South Africa during the period 1900-1930.

[Reproduced from *Union of S. Africa Annual Report of the Department of Public Health for Year ended 30th June, 1934.*]

Yu (K. Y.). *Leprosy among Natives of Manchuria.*—*Jl. Oriental Med.* 1934. Nov. Vol. 21. No. 5. pp. 67-71.

This is a brief account of four cases of leprosy among the indigenous inhabitants of Manchuria, who were probably infected during long residence in Mukden villages of Shantung mining and artisan immigrants. L.R.

GALT (Curtis M.) & YAWT (Noi). **Kiulungkiang Married Lepers' Settlement.**—*Internat. Jl. Leprosy*. Manila. 1934. Aug.–Oct. Vol. 2. No. 3. pp. 315–317.

On account of too many lepers leaving this colony in China early in 1932 married lepers were allowed to start a neighbouring village of their own on a self-supporting basis, and lepers in the colony were permitted to marry and move to the village, treatment being supplied to them as before. Only those in fairly good health, who could build a modest house and cultivate a garden, were granted such leave. It now includes forty-seven couples, together with six children taken to the village and twenty-five born there, of whom seven have been adopted by friends and 18 await adoption, which is common custom there, and it is also hoped to provide an untainted home for children. There has been only one request for return to the parent home and no financial aid has been needed, but attendance for treatment has not been very regular. The finances of the parent colony have benefited greatly, and losses of patients have been much reduced, so the experiment is being continued with an open mind as to the ultimate results. L. R.

HAYASHI (Fumio). **The Anti-Leprosy Works in Various Parts of the World as I have seen them.**—*Jl. Public Health Assoc. Japan*. 1934. Sept. Vol. 10. No. 9. pp. 1–13.

This is an interesting but diffuse account of the impressions of the author during a year's tour of a number of leprous countries, in which he bears witness to good work being done. He emphasizes the number of infections of children under leper segregation, including 38 per cent. of those born at Culion, and the importance of homes for untainted children removed as early as possible from leper parents, and elsewhere in India. He prefers the Japan solution of preventing conception by doing vasectomy on the husband before marriage is allowed. He is not in favour of the Culion parole system unless the patients are followed up, which has not yet proved feasible. The surveys in India are commended. The incidence, so common in Japan, of alopecia in leprosy is discussed and the conclusion come to that a cold climate favours its occurrence. The great decline in the mortality rates among lepers in various countries is pointed out. The value of the Mitsuda reaction is stressed. With regard to treatment he says: "The efficacy of chaulmoogra oil is an obvious fact, still there are some who doubt its value." L. R.

VELASCO (Felix). **Frequency of Leprosy among Parents and Children : its Bearing in the Transmission and Epidemiology of the Disease.**—Reprinted from *Rev. Filipina de Med. y Farmacia*. 1934. Sept. Vol. 25. No. 9. pp. 423–433. [18 refs.]

This inquiry was carried out in the Manila leper hospital among 27 adults with 125 children of whom 80 were examined; 61, or 76.3 per cent., were leprous, 22.9 per cent. being bacteriologically positive and 77.1 per cent. clinical cases. The incidence in the children was highest where one or both of the parents were positive, lower when the father is a clinical leper and least when both parents were healthy. A noteworthy feature was that the early recognizable lesions are usually found on the bare skin surfaces which during infancy are

most frequently in contact with the skin of the mother, and these are also the frequent sites in adults. "This fact seems to justify the assumption that transmission is a direct skin to skin contact between the leper and the susceptible infant or young child." Moreover, the results of leprolin tests indicate that infection most frequently takes place in infancy. *L. R.*

WAYSON (N. E.). **Leprosy with Tuberculosis in Hawaii.**—*Public Health Rep.* 1934. Oct. 12. Vol. 49. No. 41. pp. 1201-1212.

The author discusses the well-known frequency of the association of tuberculous and leprosy infections as seen in Hawaii, where DOOLITTLE obtained 75 per cent. of positive tuberculin reactions among 1,500 school children. In a group of leprous patients tuberculin reactions were about half to one-third as frequent as in other groups. The average annual death rate from tuberculosis among 155 lepers was nearly 2,000 per 100,000, against 100 in the general population. Febrile and local leprous reactions are more common in patients with tuberculous complications, namely 70 per cent. against 15 per cent. in those without this complication. The explanation of these data is not very clear except that any complicating disease tends to increase the severity of leprosy. Methods for the control and treatment of tuberculosis may have a good effect on leprosy incidence. *L. R.*

BASU (N. K.). **Deficiency of Vitamin-B₂ (G) as an Etiologic Factor in Leprosy.**—*Ztschr. f. Vitaminf.* Berne. 1934. July. Vol. 3. No. 3. pp. 194-195.

In this short note the author states that the occurrence of pellagra in lepers led him to investigate their diet in Calcutta, where it is very poor in protein and vitamin B, especially in B₂. On giving a teaspoon daily of a preparation adjusted to the strength of marmite he found after a month improvement in the sensation of nerve forms of leprosy, but no effect in nodular cases. *L. R.*

CAMPOS (Nelson de Sousa). A prova da histamina no diagnostico da lepra maculo-anesthetica. [**The Histamine Test in Diagnosis of Maculo-Anaesthetic Leprosy.**]—*Brasil-Medico.* 1934. Dec. 29. Vol. 48. No. 52. pp. 1083-1088.

The author describes the effect of the phosphate or hydrochloride of histamine, when a needle is inserted through a drop of it into the skin not deeply enough to draw blood, or when a solution of it is injected intradermally. For the test the author uses a 1 per cent. solution or 0.1 cc. of it for injection. The procedure has already been described by RODRIGUEZ and PLANTILLA [see this *Bulletin*, Vol. 29, p. 268], but these authors used a 1 in 1,000 solution and stated that reactions are not constant if stronger solutions are used.

The effect on the normal skin and on skins showing conditions of dermatitis not associated with nerve lesions is a reddening of 3-4 mm. diameter round the site of the prick in 20 seconds, followed by a wider flush in 15-30 seconds and a wheal in 5 minutes or less. In the case of leprotic maculae this reaction fails to appear and the author regards the test as one of considerable diagnostic value in early cases where bacteriological examination has proved negative. There are certain

drawbacks or limitations to its usefulness, however, for "interpretation of results is impeded in dark skins, in lesions associated with much erythema, and in dark cicatricial spots." H. H. S.

LOWE (John). **A Further Note on Nerve Abscess in Leprosy.**—*Internat. Jl. Leprosy*. Manila. 1934. Aug.-Oct. Vol. 2. No. 3. pp. 301-304. With 6 figs. on 2 plates.

This brief note is illustrated by excellent photos of the external appearances in five cases, and of a large abscess of the ulnar nerve dissected out at an operation. In Dichpali the incidence among about 5,000 lepers was 2 per cent., but half of these followed reactions induced by potassium iodide. They were met with in all the nerves most commonly affected by the disease and produced evident swellings under the skin in superficial nerves. The lepra bacillus was found in half those operated on, and in nearly every case in the neighbouring thickened portion of the nerve, together with caseous-like material. Such abscesses may occasionally perforate the skin and continue discharging for years, but they may also undergo resolution, so operations are not always required unless pressure symptoms develop; drainage is unnecessary after dissecting out the abscess material when it has escaped from the nerve sheath, as not infrequently occurs. These cases are equally common in Calcutta, but more frequently involve the subcutaneous nerves. L. R.

WADE (H. W.). **Tuberculoid Changes in Leprosy. II. Lepra Reaction in Tuberculoid Leprosy. III. The Pathology of a Nerve Abscess.**—*Internat. Jl. Leprosy*. Manila. 1934. Aug.-Oct. Vol. 2. No. 3. pp. 279-292. With 20 figs. on 5 plates; 293-300. With 12 figs. on 2 plates.

The first of these papers discusses six cases of probable lepra reaction seen in South Africa, four diagnosed as such clinically, of which two were severe, and two showing doubtful reactions, but were bacteriologically positive. One severe reaction followed the administration of potassium iodide and was of long duration. Histologically the lesions showed only tuberculoid changes with the production of epithelioid and some giant cells, together with relatively numerous bacilli for this type, but not in the form of globi, and mostly in the advancing border in the reacting cases. The prognosis of this development is thought to be unfavourable. Excellent photos accompany the paper.

III deals with the microscopical changes in nerve abscess tissue supplied by Dr. LOWE, at Dichpali [above]. This was found to present a highly organized tuberculoid granuloma, surrounded by an inner capsule of vascular lymphoid follicles, and an outer one apparently derived from the perineurium, the whole considered to be the product of a lepra reaction in a nerve and containing few or no bacilli. L. R.

PESCHKOWSKY (G. W.). Steigerung der fagozitären Aktivität der polynuklearen Leucocyten als Resultat der entzündlichen Exazerbation, und das weisse Blutbild als Ausdruck des Typus der entzündlichen Reaktion bei Leprosy. [**The Blood Picture in Leprosy.**]—*Internat. Jl. Leprosy*. Manila. 1934. Apr.-July. Vol. 2. No. 2. pp. 129-138. English summary.

The author describes the blood picture in leprosy as the result of an inflammatory reaction of the reticulo-endothelial system. The presence

of monocytosis is unfavourable as it indicates the dissemination of the disease with the formation of fresh granulomata with proliferative chronic inflammation. On the other hand, lymphocytosis is favourable in most cases, as it coincides with a period of convalescence and decrease of the inflammatory process. Polymorphonuclear leucocytosis accompanies an exacerbation of the disease with suppurative inflammation and subsequent destruction of the bacilli in the polynuclear leucocytes.

L. R.

LAI (Daniel G.). **The Dextrose Tolerance Test in Leprosy.**—*Amer. Jl. Trop. Med.* 1934. Nov. Vol. 14. No. 6. pp. 575–584. With 1 fig.

Sixty lepers and one normal control have been tested with the following results. The mean basic metabolic rate was 62·7. The fasting blood sugar rate varied from 62 to 124 mgm. per 100 cc., and averaged 88·5 mgm. The composite blood sugar curve was considered normal. During the test 58 per cent. showed glycosuria once or more. In 27 per cent. high, and in 19 per cent. flat, curves were seen, and the renal threshold was usually low. Thus, in spite of individual variations, uncomplicated leprosy tends to give a normal blood sugar curve, and glycosuria is apparently due to a low renal threshold commonly occurring in leprosy.

L. R.

SARDJITO & SITANALA (J. B.). **Additional Notes on Lepra Bacilli in the Thick Blood Drop taken from Normal-appearing Skin Areas of Lepers.**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1934. Vol. 23. No. 4. pp. 159–167. [11 refs.]

These workers conclude from their investigation that the acid-fast bacilli found in drops of blood obtained from normal looking skin of leprosy patients are derived from the circulating blood, and only to a negligible degree from the tissue fluids. This indicates that the disease is disseminated through the blood stream, but the bacilli may accumulate in the capillaries and later make their way into the surrounding tissues to start new lesions. The examination of blister fluids for bacilli is therefore not advised. They found the bacilli in thick blood preparations made by pricking the healthy skin of the ear or a finger in 85 per cent. of nodular and in 17 per cent. of nerve cases.

L. R.

MOUTOUSSIS (Konstantin). Ueber die Bazillämie bei Lepra und sonstige Befunde im Blute bei Leprakranken. Vorläufige Mitteilung. [**Bacillaemia in Leprosy.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Nov. Vol. 38. No. 11. pp. 487–494. With 5 figs.

The author records the examination of the blood of 79 lepers for acid-fast bacilli with positive results in 45 of 46 nodular cases, in 13 out of 15 with macular lesions, in 6 of 9 nerve cases, and in 8 of 9 mixed ones.

L. R.

OTA (Masao) & SATO (Saburo). **Cultivation of Leprosy Bacilli and of the Tubercle Bacillus from Leprosy Tissues.**—*Internat. Jl. Leprosy.* Manila. 1934. Apr.–July. Vol. 2. No. 2. pp. 175–192. With 12 figs. on 1 plate. [30 refs.]

After giving a short account of previous Japanese work on the subject the authors describe their own attempts to cultivate the leprosy bacillus, and lay due stress on the difficulties in deciding whether acid-fast bacilli so obtained are true lepra ones. Their work is well summarized in their own conclusions as follows:—

"1. An acid-fast bacillus cultivated from leprosy materials is not necessarily the leprosy bacillus. We have obtained cultures of the human tubercle bacillus from a clinically typical leprosy nodule and a typical leprotic lymphoma.

"2. It is very difficult to obtain the tubercle bacillus from the blood by Löwenstein's method, even with lepers having complicating tuberculosis. We used this method in 83 cases of advanced nodular leprosy, one half with pulmonary tuberculosis, and obtained no culture of the tubercle bacillus. On the other hand we cultivated twelve strains of acid-fast bacilli which were not tubercle bacilli.

"3. In one instance, four months after an acid-fast bacillus was obtained from a leper by the blood culture method, the same organism was also recovered from a nodule removed from the same patient, demonstrating that the cultures were not contaminations from outside but that the patient had a general infection with this organism. This is important evidence that the organism is the leprosy bacillus.

"4. Two other strains of the acid-fast bacillus were cultivated from nodules from two patients. It is more difficult to obtain these organisms from the nodule than from the blood, though we believe that more positive results may be obtained by improving the technic.

"5. From the results of animal inoculations and complement-fixation and skin reactions not described in this paper it seems highly possible that the strains obtained by us are *Mycobacterium leprae*.

"6. These strains may be divided into two types according to the color of the cultures, one being whitish, the other ochre or orange-colored, though these characteristics are not always constant and in some cases whitish strains change to ochre color during subcultivation. These types we call *Myco. leprae* var. *album*, and *Myco. leprae* var. *aurantiacum*, respectively." L. R.

DENNEY (O. E.). **A Microscopic Study of *Mycobacterium leprae*.**—*Internat. Jl. Leprosy.* Manila. 1934. Aug.–Oct. Vol. 2. No. 3. pp. 275–278. With 25 figs. on 3 plates.

This is a brief description of the morphology of the lepra bacillus in unstained material, and is illustrated by high magnification drawings. The beading and branching of the organisms is well brought out, and also the appearances of globi masses of bacilli, which are described as disk-like colonies of organisms surrounded by a cell membrane. The significance of the granules is still unknown. L. R.

STEIN (A. A.) & STEPÉRIN (M. I.). Die spezifische Allergie bei Leprosen. [**Specific Allergy in Leprosy.**]—*Antonie van Leeuwenhoek Nederl. Tijdschr. v. Hyg., Microbiol. en Serol.* 1934. Vol. 1. No. 3. pp. 209–218. [11 refs.]

The author reports that the injection of emulsions of leprosy nodules (leprolin) into the skin produces specific reactions. In clinical cases the

appearances of the reactions are similar to those of tuberculin. In more advanced cases the reaction varies from negative results in mixed and nodular cases to positive ones in nerve cases. Healthy persons give positive reactions. Negative results are met with in persons who have had no contacts with lepers and positive ones in those who have had such contact.

L. R.

NAKAMURA (Keiso) & KOBASHI (Shigeho). Inokulationsversuche der Menschenlepra auf Hausratten. I. Mitteilung. [**Inoculation of Leprosy to Rats.**—*Keijo Jl. Med.* 1934. Sept. 30. Vol. 5. No. 3. pp. 184–189. With 8 figs. (1 coloured) on 2 plates.

The authors report that by the inoculation into young rats of human leprosy material after damaging the nasal mucous membrane by acid an infection will result, and also by intratesticular inoculation after removal of the thyroid gland.

L. R.

JORDAN (Paul). Notas preliminares sobre o “gambá” como animal de experiência para a lepra. Pesquisa dos bacilos ácido-resistentes nos animais sãos. [**Opossum as Experimental Animal in Leprosy.**—Reprinted from *Folia Clin. et Biol.* São Paulo. 1934. No. 3. pp. 85–88. German summary.

BOVÉ in Cayenne found an opossum with mutilated toes as in leprosy, and the inguinal glands and an infiltration of the bones showed acid-fast rods. An opportunity occurred to dissect opossums but no signs of leprosy bacilli were found in the nasal mucus, glands, brain or spinal cord, or in internal organs. Fifty fleas caught on the animals were also negative. Opossums were inoculated with human leprosy material with negative results.

L. R.

JORDAN (Paul). Estudo sobre o sôro leproso. Experiencias com extractos de actinomicetos como antigenos na reacção do desvio do complemento. [**Complement Reactions in Leprosy.**—Reprinted from *Folia Clin. et Biol.* São Paulo. 1934. No. 3. pp. 81–84. [11 refs.] German summary.

The author records that lepers negative to the Wassermann reaction may yet give positive results with an alcoholic extract of actinomycetes.

L. R.

DES ESSARTS (J. Quérangal) & LEFROU (G.). Note sur le diagnostic différentiel entre les nodules élémentaires lépreux et tuberculeux dans les lésions cutanées. [**Differentiation of Skin Lesions of Leprosy and Tubercle.**—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 706–709.

This is a short note on the microscopical differences between tuberculous and leprosy lesions of the skin. The main points are that in leprosy the nodules stain more uniformly, but are more irregular in shape, affect the epidermis less with more irregular arrangement of the cells, are more vascular, contain few lymphocytes and giant cells, do not caseate and contain much larger numbers of acid-fast bacilli.

L. R.

GILLIER (R.). Formol-gélification des sérums lépreux. [**Formol-Gel Test with Leprous Sera.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 709-713. With 2 figs.

The author has applied this test in 18 lepers, 2 children living with leper parents and 30 syphilitics, and concludes that the formol-gel test is positive in Wassermann negative lepers. The optimum strength is one to two drops of formol added to 1 cc. of serum. The reaction is more rapid than with syphilitic sera. L. R.

MONTESTRUC (E.). Lèpre et séro-floculation de Vernes à la résorcine. [**Vernes Resorcin Sero-Flocculation in Leprosy.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 713-715.

This reaction consists in a flocculation of serum on the addition of 1.25 per cent. solution of resorcin due to an excess of euglobulins and pseudoglobulins; it was first used in tuberculosis. The present paper records tests in 17 nerve and 34 nodular lepers, and the conclusions are come to that it occurs only in the nodular form, and that it is of no use in the diagnosis of early cases since it only takes place in those easily recognized either clinically or bacteriologically. L. R.

RUBINO (Miguel C.). Les antigènes lipidiques d'organes dans le séro-diagnostic. Nouvel antigène de séro-floculation dans la lèpre. [**Lipoid Antigens of Organs in the Serodiagnosis of Leprosy.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 35. pp. 894-897.

This is a preliminary report on the employment of lipid alcoholic extracts of the organs of rabbits, with formalized red corpuscles of sheep as an antigen in the sero-flocculation of the serums of lepers. Extracts of the kidneys gave no reactions and those of nervous tissues slight ones, but the liver preparations were the most active. Reactions may be obtained with the sera of lepers which are negative, with those of syphilitics and other diseases. The diagnostic value of this test has not yet been worked out and purer lipoids are required than have yet been obtained. L. R.

PAIDROCK (A.) & POOMAN (A.). Die Trypanblauquaddelreaktion bei Leprösen. [**The Trypanblue Wheal Reaction in Leprosy.**]—*Internat. Jl. Leprosy.* Manila. 1934. Aug.-Oct. Vol. 2. No. 3. pp. 271-274.

This reaction is carried out by the intradermal injection of a 1 in 5,000 watery solution of trypanblue into an 8-10 mm. patch of skin in the inner side of the upper arm and also on the intrascapular portion of the back. After twenty-four hours blue staining of the whole infiltrated area is noted on the back and a ring-like staining on the upper arm, and subsequently varying degrees of diffusion and absorption of the stain are noted. Absorption is normal on both the arm and the back in the case of maculo-anaesthetic and slight cutaneous cases in 87.5 and 100 per cent. respectively, but was accentuated in 100 per cent. of advanced cutaneous cases, the total number tested being 43 lepers. Diffusion, on the other hand was normal and unaccentuated in 93.7, 100 and 92.3 per cent. of the three types in the same order as above. L. R.

MUIR (E.). **The Leprolin Test.**—*Calcutta Med. Jl.* 1934. Nov. Vol. 29. No. 5. pp. 225–226. With 5 figs. on 1 plate.

This brief note records that Hansen's leprolin has been used with advantage for intradermal injections of suspensions of 1–10 to 1–30 into leprosy lesions in patients showing acquired immunity or enhanced resistance to the disease. One infiltration may cause the disappearance of well-marked lesions and 50 per cent. of all cases are suitable; treatment is much shorter than with hydnocarpus preparations. L. R.

DUBOIS (A.) & DEGOTTE (J.). La réaction de Mitsuda dans la lèpre. [**Mitsuda's Reaction in Leprosy.**]—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 802–805.

In the Mitsuda test a suspension of broken up lepromata sterilized by boiling is injected intradermally, while Bargehr's modification is a cuti-reaction done by applying the material to an abraded portion of the skin; French observers, however, have found the latter less reliable than Mitsuda's original method, which is reported on in this note, with the use of one-tenth to one-twentieth of a cc. of a phenolized solution of lepromas in saline. A positive reaction consists of a persistent infiltration of the skin of from 1 to 10 mm. in diameter and it should be noted after one, two and three weeks. Negative results occur in active cutaneous leprosy containing numerous lepra bacilli, but both maculo-nervous cases with few or no bacilli and healthy persons give positive reactions owing to their tissues not having become accustomed to the toxic material. Tests in 171 lepers and 12 healthy subjects dealt with in this paper confirm these results. L. R.

GOMEZ (J. M.). **The Gomez Complement-Fixation Reaction in Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1934. Aug.–Oct. Vol. 2. No. 3. pp. 265–269.

Working in Brazil since 1926 the author has used glycerin broth cultures of Deycke's streptothrix incubated for 20 days at 37°C., after removal of the waxy-fatty coating by treating with olive oil and acetone until not more than 10 acid-fast bacilli are found in each microscopic field. The resulting fine whitish powder is kept in a sterile flask, and a 9 per cent. emulsion in normal saline is made and heated to 100°C. for five minutes to destroy anti-complementary reaction. 0.5 cc. of the antigen is added to 0.05, 0.1, 0.2 and 0.5 cc. respectively in four tubes and sensitized red cells added. Over 2,000 tests have been performed, including 559 lepers, 713 suspicious cases and 154 other cases. In the typical cases nodular and mixed ones gave 96.7 and 95.4 per cent., and in maculo-anaesthetic and nervous ones 65.6 and 64.8 per cent. positive reactions. In suspicious cases 54.5 per cent., in carriers 31.8 per cent. and in contacts 42.6 per cent. were positive, but none of 5 controls. In 154 other cases, mostly skin troubles, 30 reacted including tuberculosis and acne patients. Activation by 2 grains of potassium iodide daily for a week increased the reactions in 88 doubtful cases by 31, but some positive cases became negative after KI. In many positive contacts acid-fast bacilli were found in glands by puncture. L. R.

- i. SÉZARY (A.), LÉVY (Georges) & BOLGERT (M.). L'action thérapeutique du vaccin antiléproux de Vaudremer. [**Thérapeutique Action of Vaudremer's Antileprotic Vaccine.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1934. Nov. 5. 50th Year. 3rd Ser. No. 27. pp. 1372-1381.
- ii. SPITZER. Traitement de la lèpre par le vaccin de Vaudremer.—*Ibid.* Nov. 12. No. 28. pp. 1390-1391.
 - i. This vaccine is prepared by cultivating sterile fragments of leprosy nodules on an aspergillus medium, and what are considered to be evolutionary forms of the lepra bacillus are subcultivated on gelatine and sterilized by iodine to form the vaccine. Three cases treated by this vaccine are recorded with some improvement.
 - ii. This is a report on a single case treated with 26 injections of Vaudremer's vaccine in the course of six months with diminution of the discoloration and pigmentation of the skin and disappearance of infiltration of the leg. L. R.
- i. SOUCHARD (L.). Dix-huit mois de fonctionnement d'un dispensaire antiléproux à l'Institut Pasteur de Saigon. Traitement par le savon total de krabao. Considérations sur la prophylaxie de la lèpre. [**Treatment by Krabao Soap in Indo-China.**]—*Arch. Insts. Pasteur d'Indochine*. 1933. Oct. No. 18. pp. 267-277. With 11 figs. on 4 plates.
- ii. — & RAMIJEAN. Contribution à l'étude du traitement de la lèpre par les savons de "krabao." Résultats constatés après un an de traitement chez des malades anciens internés à la Léproserie de Cu-Lao-Rong.—*Ibid.* pp. 187-265.
- iii. GUILLERM (J.), BANOS (M.) & NGUYEN-VAN-LIEN. L'utilisation du "krabao" Indochinois pour le traitement de la lèpre.—*Ibid.* pp. 171-185.
- iv. PÉROT (Em.). Les espèces chaulmoogriques et, en particulier, le Krabao indochinois pour le traitement de la lèpre.—*Bull. Acad. Méd.* 1934. Nov. 20. 98th Year. 3rd Ser. Vol. 112. No. 37. pp. 602-605.

i. This paper records the well-known vegetable sources of chaulmoogra oils containing chaulmoogric and hydnocarpic acids, and the methods of preparing their therapeutic products used in French Eastern possessions. The necessity for obtaining fresh seeds of *Hydnocarpus wightiana* in India and *Hydnocarpus anthelmintica* in Indo-China is pointed out, from which the oil is obtained by pressure in the cold. In the preparation of the soaps or sodium salts the importance of neutralizing them with carbonate of soda is emphasized and also their preservation in a dry state protected from humidity.

ii. A trial of the soaps orally in 48 advanced voluntary cases of from ten to twenty years' duration in the Cu-Lao-Rong leper asylum, where no early cases were available, is recorded with full notes. The drug was given in 0.30 centigram pills, of which up to twenty were taken daily for five months, and the course repeated after two months interval, and a third course given after one and a half to two months further rest. A month after the commencement of the treatment most of the patients showed diminution of their nerve pains, but only after three months treatment was improvement in the cutaneous lesions observed in some only of the cases. Most patients only tolerated 14 to 16 pills daily

and minor digestive troubles were noted in many and considerable hepatic deficiency in some. Among 42 patients who persisted with the treatment decided amelioration was noted in 14, or 34 per cent., doubtful improvement in 6, or 15 per cent. no change in 11, or 26 per cent., and in 11 or 26 per cent. retrogression was noted. The chief difficulties in the treatment were due to the very advanced nature of the cases, with gastric intolerance in some, and associated syphilis, tuberculosis and other complicating diseases in others. The authors conclude that in about 30 per cent. of these 10 to 20 year old cases amelioration was obtained, but that by the treatment of such alone leprosy cannot be controlled; prophylactic measures are necessary, although very difficult to carry out in Indo-China.

iii. This paper deals with a trial of the soaps orally in an out-patient clinic which 67 patients attended, but only 47 at all regularly. The results were very similar to those above described in the asylum cases. Photos show great improvement in a few of the nodular cases. The method is considered to be of considerable importance.

iv. This brief note also enumerates the chaulmoogra oil bearing trees and mentions the composition of *H. anthelmintica* or Krabao oil.

L. R.

PAGET (H.), TREVAN (J. W.) & ATTWOOD (A. M. P.). **The Irritant Constituent of Anti-Leprotic Oils.**—*Internat. Jl. Leprosy.* Manila. 1934. Apr.-July. Vol. 2. No. 2. pp. 149-158. [10 refs.]

During an investigation for irritant properties of the still unidentified constituents of the total fatty acids of *H. wightiana* and sapucainha oils separated by the cold process, the authors found that the only such product was a 9 per cent. tarry fraction, which appeared to consist essentially of a lactonic acid. The ethyl esters of the crystalline acids were not rendered irritant by distillation at 350°/760 mm., but became so on long exposure in thin layers to light and air, possibly due to the production of lactonic acid.

L. R.

EMERSON (George A.). **Mechanism of the Emetic Action of the Chaulmoogrates.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Oct. Vol. 32. No. 1. pp. 238-240.

As READ has cast doubt on his own evidence as to the central emetic action of chaulmoogrates, the author has reinvestigated the matter by feeding dogs and cats, and he confirms the central action of the drug. He also found that cannabis, atropine and morphine all act in abolishing the emetic response in these animals.

L. R.

NOLASCO (J. O.). **Histologic Studies on the Plancha or Infiltration Method of Leprosy Treatment.**—*Internat. Jl. Leprosy.* Manila. 1934. Apr.-July. Vol. 2. No. 2. pp. 159-174. With 2 plates. [22 refs.]

This is a useful summary of the author's histological investigations of the effects on the tissues of the injection of chaulmoogra oil preparations in the case of lepers, non-lepers, dogs and monkeys. The ethyl esters induce a mild inflammatory reaction with an accumulation of

the drug, especially as yellowish globules in large mononuclear cells, which may persist for nine months with beneficial results. Sodium hydnocarpate and alepol cause very similar reactions together with thrombosis of the larger local vessels which limit their use, and their irritant effects appear to reside in their fatty acid radicle. Tests on monkeys indicate absorption of the drugs through the lymphatics where they may reach the lepra bacilli. Injections of the whole oil cause less cellular reaction than iodized esters. The nerve trunks were found to be unaffected. The histological changes are illustrated by camera lucida drawings.

L. R.

NOLASCO (J. O.). **Local Effects of Injection of Iodized Wightiana Ethyl Esters and Wightiana Oil around Nerve Trunks.**—*Jl. Philippine Islands Med. Assoc.* 1934. Nov. Vol. 14. No. 11. pp. 421-433. With 7 figs. [13 refs.]

This study was made on monkeys killed at various intervals after the injection of esters and wightiana oil around nerve trunks, which produced acute inflammatory reactions with fibro-cellular exudates and even pus formation. The material was phagocytosed by large mononuclears and carried up and down the limb in the loose perineural tissues, but was never found within the nerve capsule. Slight leucocytic infiltration within the sheaths indicated extension of the inflammatory process; to this the beneficial results in the relief of pains and anaesthesia after the injections is attributed.

L. R.

LABERNADIE (V.). Essais de traitement de lépreux par des injections intraveineuses d'huile de chaulmoogra (résultats obtenus après 6 mois de traitement). [**Treatment by Intravenous Injections of Chaulmoogra Oil.**]—*Ann. de Méd. et de Pharm. Colon.* 1934. July-Aug.-Sept. Vol. 32. No. 3. pp. 328-337.

The results of six months treatment by intravenous injections of *H. wightiana* oil given very slowly through a fine needle are reported. One cc. doses twice a week were used, either exactly neutralized or with the slight acidity of 3 per 100 oleic acid. No coughing or other trouble occurred after the injections nor any febrile reactions or obliteration of the veins. Both preparations gave very similar results and isolated congested nodules benefited more rapidly, while pigmentation and anaesthesia recovered more slowly, but atrophic lesions did not improve.

L. R.

MONTEL (L. R.). Traitement de la lèpre par le bleu de méthylène en injections intraveineuses. [**Treatment of Leprosy Intravenously by Methylene Blue.**]—*Bull. Acad. Méd.* 1934. Oct. 2. 98th Year. 3rd Ser. Vol. 112. No. 30. pp. 208-230. [13 refs.]

This important paper records the results of nine months trial in 172 lepers of the author's method of intravenous injections of 1 per cent. neutral methylene blue sterilized by heating on three consecutive days for one hour at 80°C., at which temperature febrile reactions are less frequent than at 120°C.

The first dose is 5 cc. increased at each injection to the limits of tolerance, which is usually between 25 and 35 cc., and given three times

a week up to 18 doses, and the courses repeated after intervals of 20 days. All the dermal leprous lesions retain the dye and stand out clearly so that the injection may be of diagnostic value as regards slight lesions. The first effect is the cessation of neuralgic pains with improved sleep and appetite and general condition. In a few cases fever results with congestion of the skin lesions followed by retrogression. Further extension of the lesions is arrested and thickening and oedema subside. The drug does not cause albuminuria. Recent lesions subside first with intense desquamation of the skin. Infiltrated patches may take four months for the thickening to disappear and the older lesions may take still longer, especially actual nodules, and after eight months treatment only partial subsidence of old fibrous nodules has been observed. On the other hand, ulcers, blisters, etc., heal rapidly and cease to discharge lepra bacilli and perforating ulcers are also very beneficially affected, nine out of ten such ulcers having healed in from two weeks to three months. Equally important is the frequent cessation of the discharge of lepra bacilli from the nose, greatly diminishing the infectivity of the patients. In nerve cases, in addition to the cessation of pain, the extension of the skin lesions is arrested and the thickened edges of tuberculoid lesions and thickening of superficial and trunk nerves subside. The treatment has thus been beneficial in all types of leprosy and it can be combined with chaulmoogra oil medication during the intervals in the methylene blue injections with advantage. L. R.

- i. FREVILLE (L. H. F.). Recherches expérimentales sur les réactions produites par les injections intraveineuses de bleu de méthylène dans la lèpre. [**Reactions produced by Intravenous Injections of Methylene Blue.**—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Aug.-Sept. Vol. 12. No. 7. pp. 615-621. With 1 chart.
- ii. MONTEL (M. L. R.). Rectification de priorité à propos du bleu de méthylène dans le traitement de la lèpre. [**Priority in the Treatment.**—*Ibid.* p. 622.
- iii. ——. Traitement de la lèpre par le bleu de méthylène en injections intraveineuses.—*Ibid.* pp. 623-646. [13 refs.]
- iv. BIGOT (A.) & LE-VAN-TRIEN. Trois cas de lèpre traités par la méthode de Montel, au bleu de méthylène.—*Ibid.* pp. 734-739.

i. The paper of Freville deals with the reactions met with after intravenous injections of methylene blue by Montel's method in 150 cases. Cardiac syncopal attacks were occasionally met with and were not prevented by adding adrenalin, so the injections should be given with the patient recumbent. Febrile reactions were also met with after the use of solutions sterilized at 80°C., but solutions prepared without heat by the use of previously sterilized materials caused very little reaction of any kind. The drug can also be given in a 1 in 20 solution intramuscularly, which produces blue staining of dermal lesions more slowly than after their intravenous use.

ii. In this brief note Montel points out that G. A. RYRIE tried intravenous injections before him, but did not apparently note benefit from methylene blue as it is not one of the dyes he advises in leprosy treatment.

iii. The third of these papers is the same as that reviewed above.

iv. Brief notes of three cases treated with immediate benefit by Montel's method, which the authors propose to follow up. L. R.

- i. MONTEL (M. R. L.). Les critères cliniques de l'action des traitements antilépreux. [**Methylene Blue Treatment.**]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. June-July. Vol. 12. No. 6. pp. 559-565.
 - ii. — & TRUONG-VAN-QUE. Un cas de lèpre généralisée à poussées aiguës traité par le bleu de méthylène. Observation et bilan après 153 jours de traitement.—*Ibid.* pp. 566-582. With 4 figs.
 - iii. DOROLLE (P.), NGO-QUANG-LY & TRAN-VAN-TAM. Premiers résultats dans le traitement de la lèpre par le bleu de méthylène (méthode de M. L. R. Montel).—*Ibid.* pp. 609-611.
- i. This paper repeats points already dealt with above.
 - ii. This is a detailed account of the treatment of a girl of 17 with extensive mixed lesions, which greatly improved after 153 days of injections of methylene blue alternating with chaulmoogra preparation.
 - iii. Four cases of leprosy benefiting much from methylene blue treatment and confirming MONTEL'S work. L. R.

AFANADOR (A.). Traitement de la lèpre par les injections intraveineuses de bleu de méthylène. [**Methylene Blue Treatment.**]—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 805-806.

This is a brief report on 20 cases of leprosy treated by Montel's method in a sanatorium at Valbonne by the injection intravenously of a total of 280 cc. of the 1 per cent. solution in 30 days giving 3 injections weekly. The immediate effects were similar to those described by MONTEL, but the time under observation was too short to allow of any modification of the zones of anaesthesia and atrophy. L. R.

LEGGATE (James). **Bonney's Blue Solution in the Treatment of Leprosy.**—*Leprosy Review*. 1934. Oct. Vol. 5. No. 4 pp. 161-162.

The author has used this treatment with success in ten advanced cutaneous cases of leprosy. Brilliant green and crystal violet, of each 0.5 gm. in absolute alcohol 25 cc. and distilled water 2,500 cc., sprayed on leprosy ulcers, and lint soaked with it applied at night, removed suppuration and induced healing. Intradermal injections of the solution were less rapidly beneficial in hard nodules and more quickly so in soft ones, followed by its intravenous use, alternating with iodized esters. In nerve cases the results were not so striking, but laryngeal, throat and nose conditions have responded well. L. R.

RYRIE (Gordon A.). **On the Use of Fluorescein and Phthallic Acid in Leprosy.**—*Internat. Jl. Leprosy*. Manila. 1934. Apr.-July. Vol. 2. No. 2. pp. 139-147.

The author records that the most stable results obtained from the intravenous injection of various aniline dyes followed the use of fluorescein in sixty-four cases treated for four months. In about 60 per cent. clinical and microscopical examinations of the lesions showed a greater or less specific response, but the improvement rate dropped to 43 per cent. on continuing the treatment for four months. In order to ascertain which constituent of the dye was effective nine cases were treated with one of its constituents, resorcin blue, with negative results, but in 16 patients treated for two months with intravenous injections of another constituent, phthallic acid, greater or less response was observed in 62 per cent., so this is considered to be the active part of

the dye. It is noted that hydnocarpus esters appear to be better tolerated after a course of fluorescein, but that very little evidence was obtained of the beneficial effect of the dye in advanced cases of leprosy.

L. R.

EMERSON (George A.) & ANDERSON (Hamilton H.). **Toxicity of Certain Proposed Antileprosy Dyes : Fluorescein, Eosin, Erythrosin, and Others.**—*Internat. Jl. Leprosy*. Manila. 1934. Aug.-Oct. Vol. 2. No. 3. pp. 257-263. [16 refs.]

The authors state that possibly dangerous doses of certain dyes have been used by RYRIE intravenously in leprosy, so their toxicity has been investigated with the following results.

"Fluorescein, eosin, erythrosin and methylene green were found to be lethal at 300, 350, 200 and 150 mgm. per kilogram, respectively, when administered intravenously to rabbits, and at 600, 500, 300 and 125 mgm. per kilogram intraperitoneally in rats. Methylene green is lethal for anesthetized cats in doses of 50 to 75 mgm. per kilogram. Orally in rats these dyes are tolerated in doses of 1.0 gm. per kilogram with the exception of methylene green, which killed 2 of 5 rats at 500 mgm. per kilogram. Data are presented on the chronic toxicity of trypan blue, gentian violet, brilliant green and mercuric bichloride. Three of 6 rabbits dying under repeated intravenous administrations of trypan blue had received a total cumulative dose, approximately equivalent to but one acute lethal dose, i.e., 120 to 150 mgm. per kilogram. The dangers of repeatedly using high doses in human lepers, the superiority of oral administration over intravenous, and the danger of certain synergizing agents, including photodynamic effects are discussed."

L. R.

PEREIRA (O. Loyola). **On the Effects of Anti-Variollic Vaccination in Lepers.**—Reprinted from *Antiseptic*. 1934. July. 4 pp. With 1 plate.

This is a brief description of the well-known severe febrile and local reactions often following vaccination of lepers against smallpox; 15 of 24 vaccinated lepers showed such reactions with great debility.

L. R.

PALDROCK (A.). **Durch spezifische Behandlung von Lepra geheilt.** [**Leprosy cured by Specific Treatment.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Jan. Vol. 39. No. 1. pp. 23-25. With 1 fig.

This is a short account of a further case of leprosy treated successfully by the author's method of local applications to the skin lesions of carbonic acid snow and injections of the gold preparations solganal and lopion.

L. R.

WATANABE (Y.). **Experimental Studies on the Lepra Bacillus. (Part I.) Inoculation Test with the Bacillus of Rat Leprosy. (Part I.)**—*Kitasato Arch. Experim. Med.* 1934. Oct. Vol. 11. No. 4. pp. 259-276.

After references to earlier Japanese work the author records his own experiments on rats and white mice by inoculation and ingestion of the rat leprosy bacillus. The results in rats were very similar to those of previous workers, local lesions developing at the site of subcutaneous injection in two weeks to three months and inconstant extension to internal organs. Orally infection was slight without involvement of the mesenteric glands. In the mice subcutaneous inoculation

only led to enlarged axillary glands containing acid-fast bacilli. Intravenous injection also showed slighter changes in the internal organs than in rats, but intraperitoneal injection involved the mesenteric glands, liver and spleen, and subinoculation caused similar changes.

L. R.

BERNY (P.). Echec de la transmission aux lapins et aux cobayes des bacilles de la lèpre des rats. [**Bacilli of Rat Leprosy not Transmissible to Rabbits and Guineapigs.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 717-719.

The author reports the production in rabbits and guineapigs injected with rat leprosy bacilli of thickening, sometimes going on to abscess formation before resolving. Acetone extracts may also produce abscesses at the site of injection, in some of which tubercle bacilli were found. Phagocytes containing acid-fast bacilli were also met with, but bacilli taken from animals on the 74th day and injected into rats disappeared without producing infection.

L. R.

ATKEY (O. F. H.). The Distribution of Leprosy in the Sudan with Reference to Climate and Diet.—*Internat. Jl. Leprosy*. Manila. 1934. Apr.-July. Vol. 2. No. 2. pp. 193-200. With 1 map in text. [See this *Bulletin*, Vol. 31, p. 542.]

GUERRIERI (Tito). Contributo allo studio sulla lebbra dei ratti.—*Arch. Ital. Sci. Med. Colon.* 1934. Nov. 1. Vol. 15. No. 11. pp. 801-827. With 4 figs. [22 refs.] English summary (6 lines).

MENDIOROZ (Julio). Estado de la lepra en Salta en 1933.—*Prensa Méd. Argentina*. 1934. Dec. 19. Vol. 21. No. 51. pp. 2415-2423. With 3 figs.

SLEEPING SICKNESS.

DUREN (A.) & VAN DEN BRANDEN (F.). Sur un cas de trypanosomiase humaine à évolution latente. [**Sleeping Sickness of Slow Evolution.**].—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 437–438.

Details of two cases are given. A European who had left the Congo 7 months previously and had not complained of any symptoms was found by chance to have an erythematous eruption, enlarged glands, with trypanosomes in the blood and gland juice. The cerebrospinal fluid showed considerable changes. This was a case which was latent from the point of view of subjective symptoms, but of normal evolution.

The second case was, however, more characteristic. The authors were consulted in May, 1934, by a man who had returned to Belgium from the Congo in November, 1932. During the first few months after his return from the tropics he suffered from slight fatigue, but improved with Fowler's solution. In November, 1933, he again felt tired, but did not consult a doctor. When he was seen by the authors in May, 1934, he was more definitely fatigued and had tachycardia. No other clinical sign or symptom was discovered, but trypanosomes were found in the blood. Careful interrogation indicated that the patient was probably infected in April 1932, that is 25 months before a diagnosis was made, and 20 months before there were any disquieting symptoms. A course of 3.5 gm. of Bayer and 21 gm. of tryparsamide was given. At the end of July, 15 days after cessation of treatment, spinal puncture revealed a normal cerebrospinal fluid.

W. Yorke.

SICÉ (A.) & MERCIER (H.). Trypanosomiase nerveuse et tuberculose. A propos d'un double échec de la cure tryparsamique. [**Nervous Trypanosomiasis and Tuberculosis.**].—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 924–929.

Details are given of two advanced cases of sleeping sickness in which treatment by tryparsamide caused latent tubercular lesions to light up with the production of severe general symptoms.

W. Y.

BERTRAND (Ivan), BABLET (J.) & SICÉ (A.). Lésions histologiques des centres nerveux dans la trypanosomiase humaine (à propos de deux cas mortels non traités). [**Histological Lesions of the Central Nervous System in Human Trypanosomiasis.**].—*Ann. Inst. Pasteur.* 1935. Jan. Vol. 54. No. 1. pp. 91–144. With 13 figs. & 3 plates. [52 refs.]

A detailed account is given of the histological changes found in the central nervous system of two untreated cases of sleeping sickness.

The paper opens with a lengthy résumé of the work of previous investigators, and this is followed by a detailed history of the two cases examined. The history and the macroscopic findings at the post-mortems showed that the two cases differed considerably. The pathological changes in the first case were much more pronounced, and there was unquestionable evidence of a diffuse leptomeningitis, whilst in the second case the leptomeningitis was scarcely noticeable.

It is almost impossible to give an adequate summary of the lengthy description of the histological findings, and the paper must be consulted in the original by those interested.

The following are the authors' conclusions :—

From the very first sleeping sickness is a diffuse meningo-encephalitis, the infiltrative character of which is very marked. The perivascular lesions exhibit a predominance of plasma cells not encountered in any other infection. The white matter is particularly rich in vascular lesions. There is no question, however, of a leuco-meningitis analogous to that seen in Schilder's disease.

The cellular elements of the infiltrations have a complex origin. In addition to strictly nervous and microglial elements there are a large number of plasmocytes and of histiocytes of adventitious or meningeal origin. The infiltrations are then partly glial and partly mesenchymatous.

The morula cells of Mott are strictly identical with the fuchsinophil cells of Russell. Without being able to state the exact chemical constitution of their inclusions, there is no doubt that they are derived exclusively from the plasmocytes. The neuroglia cells never exhibit inclusions of this kind. The histiocytes and the microgliocytes are able to engulf the bodies of morula cells when they have reached a sufficiently advanced degree of disintegration.

The neuroglial formula of trypanosomiasis depends essentially on the length of its evolution. The presence of numerous cells *en bâtonnet* of Nissl in the substance of the grey cortex and even in the white matter indicated a chronic process, but is in no way pathognomonic.

The numerous amoeboid cells of the neuroglia, which are seen in the white matter, sometimes in great number, in preparations impregnated with gold sublimate (Ramon Cajal) show prolongations, hypertrophied but free, contrary to the classical opinion.

Clasmatodendrosis is rare and generally limited to the suckers of the fibrous neuroglia.

The cortical glia is much less attacked than in general paralysis.

The neuroganglion lesions of the cerebral cortex consist chiefly of an acute tumefaction. The appearances of liquefaction indicative of a grave and irreversible degeneration are absent, in contrast to what is seen in paralytic dementia.

W. Y.

MACKIE (F. P.). **The Jarisch-Herxheimer Reaction in Trypanosomiasis. With a Note on the Morular Cells of Mott.**—*Trans. Roy Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 377-384. With 2 plates. [25 refs.]

An account is given of the post-mortem changes found in the brains of two men who died of *rhodesiense* sleeping sickness. Each exhibited features which justify a special note, in the first regarding the Jarisch-Herxheimer reaction, and in the second the "morular bodies of Mott."

Case I.—Contracted sleeping sickness in Rhodesia about a year previously, but, as the nature of the illness had not been suspected, he had been given no specific treatment until a few weeks before death, when he received 3 doses (total 1 gm.) of N.A.B. on another assumption. On admission to hospital *T. rhodesiense* was scanty in the blood and cerebrospinal fluid. The day following admission the patient was given an intravenous injection of tryparsamide, grams 2. The temperature, which was high at the time, continued to rise and reached 107.2°F. an hour before death. The patient became comatose, with marked tremor of the right leg and arm; nuchal rigidity and Kernig's sign were present; and the pupils were dilated and fixed. Lumbar puncture was performed. The cerebrospinal fluid was clear, but the pressure was increased, as were also the globulin and lymphocyte contents.

Post-mortem.—A detailed account is given of the findings at the autopsy. On opening the skull there was a gush of blood-stained cerebrospinal fluid. The membranes were congested; there was a considerable amount of blood-stained oedema over the Rolandic areas on the left side, and there was gelatinous oedema under the pia over the vertex. On cutting through the base of the ganglia there was seen to be a wide area of deep red haemorrhagic softening occupying the anterior half of the caudate nucleus and the anterior and lateral aspects of the lenticular nucleus. These appearances were due to the confluence of punctate haemorrhages producing a massive effect.

Case 2.—This was a chronic case infected in Northern Rhodesia in 1928. The patient had suffered from five relapses and had received, during the course of his illness, 36 grams of Bayer 205 and 33 grams of tryparsamide.* The patient failed to respond to treatment and death occurred without any signs of a cerebral catastrophe, such as occurred in the former case.

A detailed account of the post-mortem findings is given.

In discussing the Jarisch-Herxheimer reaction, the author points out that this phenomenon was first described by JARISCH (1895) as an exacerbation of cutaneous syphilides resulting from mercurial treatment. HERXHEIMER and KRAUSE (1902) showed that the reaction was not confined to cutaneous manifestation, but was a systemic reaction, which caused a general "flare-up" of syphilitic activity, wherever such lesions were present, and that it was much more common and severe as the result of treatment with organic preparations of arsenic. Clinically, the reaction may be nothing more than a slight rise of temperature with an exacerbation of local signs, or there may be alarming symptoms, such as excruciating headache, vomiting, tremors, epileptic convulsions, coma, and death.

Autopsy in such cases may reveal nothing more than vaso-dilatation of the cerebral meninges with irregularly distributed areas of cerebral softening. In some cases these were associated with punctate haemorrhages or small focal haemorrhages in various parts of the cerebrum. The various hypotheses which have been advanced to explain the Jarisch-Herxheimer reaction are briefly discussed. There is no doubt that a genuine Jarisch-Herxheimer reaction occurs in human sleeping sickness, but this reaction is confused or over-shadowed by the more frequent therapeutic catastrophes which are almost certainly due to toxic alterations in the drugs used.

Morula cells.—These were first described by MOTT (1906) as follows:—" . . . large, round or oval cells with the nucleus staining deep blue and pushed up to one end or pole; the cytoplasm consisting of a number of clear spherules, staining by eosin giving the cell a mulberry appearance: hence I have called these cells 'morular cells'. They correspond to the Körnchenzellen of Alzheimer. The appearance of these cells suggests degenerated plasma cells. Similar cells are seen in the degenerated structures of infected lymphatic glands."

PERUZZI has given a full account of their distribution, structure and probable origin. He describes them as cells with fuchsinophilic hyalin globules, which after destruction of the protoplasm and rupture of the cell present all the characters of Russell's bodies. He thinks that though they may have a multiple origin in trypanosomiasis, they are generally derived from the neuroglia, and he believes that they are indicative of the presence of a severe virus causing nerve cell destruction.

* The original has "grains" in each instance; a correction is published in the succeeding number of the Transactions.

In Mackie's case morula cells were most numerous in the cellular exudate of the pia and in the perivascular cuffs, but they were also seen in the brain substance, not obviously in connexion with blood channels. They are also found occasionally in other organs, and similar bodies have been seen by Mackie in normal intestinal mucosa. This fact excludes the assumption that their origin is invariably from neuroglia cells.

W. Y.

CORSON (J. F.). **Experimental Transmission of *Trypanosoma rhodesiense* through Antelopes and *Glossina morsitans* to Man.**—*Jl. Trop. Med. & Hyg.* 1935. Jan. 1. Vol. 38. No. 1. pp. 9-11.

A strain of *T. rhodesiense* taken from man a year previously was found to be still infective for man after a number of cyclical passages through *G. morsitans* and dik-diks. It has been previously shown by Corson that *T. rhodesiense* could be maintained in sheep and goats for nearly two years without losing its transmissibility by *G. morsitans* or its infectivity for man. In the present experiment, *T. rhodesiense* was transmitted by single isolated infective *G. morsitans* from antelope to antelope, and finally to man.

The experiments commenced on July 24, 1933, when the blood of a Rhodesian sleeping sickness patient was inoculated into a number of guineapigs. From one of these guineapigs a fly was infected, and this in due course infected a dik-dik. The strain was then passed through fly—dik-dik—fly—dik-dik—fly. During the year, therefore, the strain had passed through a guineapig, 4 tsetse flies, and 3 dik-diks. The last fly was fed on a volunteer on the 27th July, 1934. A ring was drawn round the site of the bite with silver nitrate. On the 5th day, a slightly red spot was noticed within the ring. On the 6th day the spot was about a $\frac{1}{4}$ inch in diameter and somewhat raised and congested, and the skin felt thickened. A stained thick blood film showed no trypanosomes; the patient felt well. On the 7th day the spot was $\frac{3}{8}$ inch in diameter and slightly painful and tender, and the blood was found to contain trypanosomes.

W. Y.

CORSON (J. F.). **Resistance of White Rats to Infection with *Trypanosoma rhodesiense* through eating Infected Tissues of Rats.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. p. 589.

After referring to the work of DUKE, METTAM, and WALLACE [*ante*, p. 33] on the infection through the mucous membrane of the mouth by feeding kittens on the carcasses of rats infected with *T. brucei*, Corson states it is important in experimental work to know whether such accidental infections may occur. He states that in his experiments during the last 8 years over 1,000 white rats have been infected with *T. rhodesiense* or *T. brucei*, but although a stock of about 1,000 rats is usually kept on the premises, no case of accidental infection has occurred.

An experiment is described in which various parts of the body, viz., liver, spleen, kidneys, heart, lungs, and hind-legs, of rats heavily infected with *T. rhodesiense* were given to healthy rats to eat. The work was done under careful supervision, each rat being able to eat its portion undisturbed. Of the 52 rats so fed, none became infected.

From this Corson concludes that it is unlikely that experiments with *T. rhodesiense* and white rats will be affected by accidental infection of the rats through eating the carcasses of other rats. W. Y.

CORSON (J. F.). **The Influence of the Dose of Trypanosomes and of the Body Weight in Experimental Infections of White Rats with *Trypanosoma rhodesiense*.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 525–534. [13 refs.]

Results are recorded in this paper of a considerable number of observations designed with the object of ascertaining whether the number of trypanosomes injected, and the body weight of the animal, had any effect on the resulting infections of white rats with *T. rhodesiense*.

In the first experiments 10 rats, each weighing approximately 100 gm., and 10 weighing about 50 gm. each, were inoculated subcutaneously with 100,000 trypanosomes. The results, which are set forth in a table, show that the incubation period and duration of life are about the same in both series. A series of experiments were then performed with the object of ascertaining the influence of the number of trypanosomes injected. These vary from 100,000 to 100. The experiments show that within these limits the number of trypanosomes had little, if any, influence on the incubation period and the duration of the infection. The experiments show, however, that it is important to introduce a certain amount of serum into the diluting Ringer-glucose solution, as this solution, in the absence of protein, will not support trypanosomes for any length of time. [Attention has already been drawn to this fact by the reviewer and his colleagues.]

Corson points out that in his experiments with *T. rhodesiense* the bite of an infected *G. morsitans* has never failed to infect normal white rats, and the incubation period and duration of the disease have been very similar to those observed after infection with a syringe. A long series of observations on this point is summarized in a table. In 80 per cent. of the rats mentioned in this table the incubation period was either 4 or 5 days, and the duration of life was from 20 to 30 days. The variations in the duration of life can be explained by differences in the resistance of individual rats. W. Y.

LAUNOY (L.). Incubation clinique et pouvoir infectant du sang, dans l'infection expérimentale à *Trypanosoma congolense* du cobaye. [**Clinical Incubation and Infecting Power of the Blood in Experimental Infections of Guinea-pigs with *T. congolense*.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 37. pp. 1047–1049.

In a previous communication the author has shown that the blood of guinea-pigs, infected by intraperitoneal inoculation of 3 or 4 million trypanosomes, was infective long before parasites could be discovered microscopically. He calls the period between inoculation and infectivity of the blood "bacteriological incubation," and that between inoculation and microscopical discovery of the parasites in the blood "clinical incubation." In certain cases, the former period was only 8 hours, whereas the latter was between 6 and 9 days.

In the present work the author has inquired whether the "bacteriological incubation" was modified by the number of trypanosomes introduced into the peritoneal cavity. The results of his experiments are summarized in tables. With two exceptions the blood of

every animal which had received 70,000 or more trypanosomes was infective within 24 hours. Of the seven guinea-pigs which received 11,750 trypanosomes, the blood of only one was infective under 30 hours, whilst in none of those which received only 1,175 trypanosomes was the blood infective within 24 hours. The author points out, however, that one must not conclude from this that the blood of guinea-pigs which have been given only 1,175 trypanosomes is really non-virulent after 24 hours. It takes about 2 hours to count the parasites and make the various dilutions, and during this period many of the trypanosomes are damaged by the physiological saline used for diluting. Nevertheless, this relatively small number of trypanosomes suffices to infect, and the "clinical incubation" is not very different from that observed after massive injections. W. Y.

LAUNOY (L.) & ANCELOT (A.). Sur le pouvoir infectant, après différents traitements, du sang de souris infectées par *Trypanosoma congolense*. [The Infectivity after Different Treatments of the Blood of Mice infected with *T. congolense*.]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 4. pp. 328-330.

Groups of mice heavily infected with *T. congolense* were treated with Bayer 205, tryparsamide and the sodium salt of antimony thiomalate. At various periods, 2 to 25 hours, afterwards the blood was injected into healthy mice by one of the following three routes: intravenous, intraperitoneal, or subcutaneous. Of the mice injected intravenously all except one became infected, and the same applied in the case of those injected intraperitoneally; but of the mice injected subcutaneously only 8 of 44 became infected. Very similar results were obtained from mice which received synergic treatment, *i.e.*, tryparsamide 0.06 gm. + Bayer 0.005 gm. or the antimony compound 200 γ + Bayer 0.005 gm.

The authors believe that this curious phenomenon is due to a particularly energetic defensive reaction, which is brought into operation on subcutaneous injection. W. Y.

VAN DEN BRANDEN (F.). Essais comparatifs du traitement des rats blancs infectés de *Trypanosoma congolense*, par l'orsanine sodique (270 Fournau) et par le tryponarsyl. [The Treatment of Rats infected with *T. congolense* by Orsanine and Tryponarsyl respectively.]—*Ann. Soc. Belge de Méd. Trop.* 1934. Sept. 30. Vol. 14. No. 3. pp. 375-378.

It is well known that *T. congolense* infections are very resistant to arsenicals, and, therefore, in order to ascertain whether orsanine possesses a greater trypanocidal activity than tryponarsyl, the author has examined the effect of each on white rats infected with this parasite.

In the first experiment 6 infected rats weighing between 100 and 120 gm. were given 0.1 gm. of orsanine and 6 similar animals 0.2 gm. of tryponarsyl; the rats given tryponarsyl were not sterilized, whilst those given orsanine were sterilized, but were poisoned by the drug and died within 36 hours. In a second series of observations the dose of orsanine was reduced to 0.05 gm.; this dose was tolerated and caused the disappearance of trypanosomes from the blood for a period of 10 days. It follows that for white rats infected with *T. congolense* orsanine is more active than tryponarsyl. W. Y.

VAN DEN BRANDEN (F.) & POTTIER (R.). L'hexaméthylène tétramine associée à la tryparsamine dans le traitement de la trypanosomiase.—Contrôle biologique du trypanurile. [**Hexamethylene Tetramine (Urotropine) in Association with Tryparsamide in the Treatment of Trypanosomiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 499–502.

In view of the statement of LIEURADE that the association of urotropine with tryparsamide increases the action of the latter in sleeping sickness [*ante*, p. 19], the authors have examined the point in rats infected with *T. congolense*.

Ten rats were given trypanarsyl alone, 0.25 gm. per 100 gm. of body weight; 10 other rats were given 0.25 gm. of urotropine followed 3 hours later by 0.25 gm. of trypanarsyl. No difference was noticed between the results given by the two forms of treatment. In a second group of experiments the procedure was similar, except that 0.5 gm. of trypanurile was given instead of the 0.25 gm. of urotropine. Trypanurile is a product of l'Union Chimique Belge, containing equal parts of trypanarsyl and hexamethylene tetramine. Here again no advantage occurred from the addition of urotropine. The authors accordingly conclude that hexamethylene tetramine does not re-inforce the action of trypanarsyl in *T. congolense* infections of rats. W. Y.

GOLDIE (H.). Effet du plasma, traité par le moranyl, sur la coagulation du sang. [**The Effect of Plasma treated with Moranyl in the Coagulation of the Blood.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 33. pp. 677–681.

If 2 cc. of 0.9 per cent. solution of moranyl is added to 8 cc. of blood just removed from the vein of a horse, coagulation is certainly prevented, but 1 cc. to 1.5 cc. only prevents coagulation sometimes. When 2 cc. ("dose certaine") is used, the plasma remains fluid, and after 24 hours in the ice-chest can be removed from the red cells. Liquid plasma containing the smaller amount of moranyl, viz., 1 cc. to 1.5 cc. ("dose limite"), coagulates after the addition of thrombine, but the other factors concerned in coagulation, viz., fibrinogen, calcium and cytozyme, exert no influence on the plasma. The author then goes on to compare oxalated plasma with moranylized plasma; the paper is of a rather technical nature and should be consulted in the original by those interested. W. Y.

- i. FISCHL (Viktor) & SINGER (Ernst). Die Wirkungsweise chemotherapeutisch verwendeter Farbstoffe. [**The Mechanism of Action of Chemotherapeutic Dyes.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1934. Sept. 22. Vol. 116. No. 4. pp. 348–355. With 2 figs [18 refs.]
- ii. SINGER (Ernst) & FISCHL (Viktor). Weitere Versuche ueber die Wirkung von Arzneimitteln in vitro. [**Further Experiments on the Action of Drugs in vitro.**]—*Ibid.* pp. 356–360. [15 refs.]

i. In this paper the authors consider the mechanism of the action of certain dyes which are known to exert a trypanocidal activity. v. JANCsó has laid down that the trypanocidal activity of dyes is parallel with their absorption by the parasites and with their

photodynamic and *blepharocidal action [see this *Bulletin*, Vol. 29, p. 646]; in the case of resistant trypanosomes all four factors, cure, absorption, photodynamic action, and blepharocidal action, are inhibited.

After summarizing various observations which seem to throw doubt on the validity of v. Jancsó's hypothesis, the authors state that the necessity of re-investigating the mechanism of action of dyes is shown by the fact that they themselves have proved that in the case of metallic compounds the curative mechanism is a complex process consisting of 3 phases—(1) A physico-chemical adsorption of the substance by the cell of the pathogenic organism, (2) a change in this adsorbed substance as a result of the vital activities of the cell, resulting in the formation of an actual poison; and (3) finally the completion of cure by the immune substances of the organism of the host [this *Bulletin*, Vol. 31, p. 851]. It is a matter of importance to discover whether in the metal-free chemotherapeutic substances—of which the most characteristic are the dyes—the 1st and 2nd phases fall together or whether they are separate.

The most obvious criticism of the investigations of v. JANCsó and of those who followed him is that they failed to use suitable controls, *i.e.*, substances which not only exhibit the necessary fluorescence, but which, although chemically closely related to trypaflavin, have no therapeutic action. Atebrin fulfilled these conditions and was selected as the most suitable control substance. In a table the chemical constitution and the various physical properties (especially as regards fluorescence) of trypaflavin and atebrin are compared, and data are given regarding the doses—toxic, tolerated, curative, effective, etc.—of the two compounds for mice infected with nagana and birds infected with malaria.

Comparable investigations with the two dyes gave the following results:—

(a) Some minutes after treatment of a nagana mouse with the tolerated dose of trypaflavin the trypanosomes when examined by the usual dark-field method exhibited, as stated by v. Jancsó, strongly illuminated blepharoplasts; under "interference" conditions or with fast strains the phenomenon was not observed. After injection of the tolerated dose ($\frac{1}{2000}$ gm.) of atebrin the trypanosomes were seen to be filled with numerous illuminated particles, but after injection of $\frac{1}{2000}$ gm. (*i.e.*, the tolerated dose of trypaflavin) nothing unusual was seen. This observation shows the specific affinity of trypaflavin for the blepharoplast and the storage of the inactive atebrin in the protoplasm of the parasites. But it cannot be decided from this whether the illumination of the blepharoplast is due to the elective storing of the drug in this structure or whether it is due to irritation. The authors do not believe that the blepharocidal action can be identical with the curative action.

(b) Observation of coverslip preparations, or dry smears of the blood, with the fluorescence microscope shows that both the active trypaflavin and the inactive atebrin are stored in the whole trypanosome body in exactly the same way.

(c) If the trypanosomes from the total blood of a mouse were collected 20 mins. after a dose of trypaflavin they were found to be coloured deep yellow, whilst after atebrin they were just as white as from an untreated animal. The fluorescence microscope, however, shows that this is only due to the weaker intensity of the atebrin stain.

These observations show that with trypaflavin, and the metal-free chemotherapeutic substances, the binding of the drug on the parasite

* A convenient abridgment of Blepharoplasticidal.

is indeed an indispensable procedure for specific action, but that it is not identical with it. This agrees with what the authors have previously found with the metallic compounds.

The authors object to the expression "lethale Lichtzahl" used by VON JANCsó in his photodynamic studies. They state that there is no relationship between the motility and infectivity of a trypanosome; and consequently it would be more correct to speak of "immobilisierende Lichtzahl." An experiment was conducted to ascertain whether the trypanocidal action *in vitro* of trypaflavin was only due to a photodynamic cause. The whole experiment was conducted in the dark. Trypanosomes from mice infected respectively with the normal and trypaflavin-resistant strains were kept *in vitro* in 20000 solution of trypaflavin. After 15 minutes the normal trypanosomes were completely immobilized and granular, whilst the resistant parasites were unchanged and feebly motile; 0.2 cc. of each suspension was then injected into healthy mice. Under these conditions, in which light was almost completely excluded, neither the normal nor the resistant strain produced infection. In a similar experiment with atebirin both normal and fast strains exhibited normal appearances and motility after 15 minutes, but they displayed a markedly decreased infectivity.

The authors believe that from the experiments they have succeeded in demonstrating that curative action, trypanocidal action *in vitro*, and photodynamic action are completely independent of one another; the sole common factor in these phenomena and in blepharocidal action is the previous incorporation of the substance in the body of the parasite.

Analogous experiments were performed with atebirin and trypaflavin in bird malaria, and also with atebirin in human malaria.

ii. In this paper the authors have attempted to go further into the question whether any relationship exists between absorption of drugs by parasites and their destruction. In a table it is shown that if equal quantities of *Spirochaeta recurrentis*, *Proteus* sp., erythrocytes, collodion and animal charcoal are placed in a solution of 0.1 per cent. atoxyl for 1 hour they absorb considerably less arsenic than if they were placed in a 0.1 per cent. solution of atoxyl which had previously been digested with liver.

The next question which was investigated was the constituent of liver, which is responsible for this activating action on atoxyl and similar phenyl arsenic acids. In addition to cystin (not cystein) and those substances, viz., glutathion and glycogen in which liver is rich the authors investigated thioglycollic acid and sodium thioglucose, and also mouse red cells and, on account of its high glutathion content, an emulsion of the calf's eye lens. Of all these substances it was found that glutathion alone exerted the activating influence on atoxyl for trypanosomes and spirochaetes. Other reducing substances known to be in the animal body are ergothionin, Vitamin B₂ and ascorbic acid (Vitamin C).

Experiment showed that ascorbic acid (1:800) killed trypanosomes *in vitro*, but had no action on spirochaetes. A mixture of atoxyl and ascorbic acid damaged the trypanosomes, but did not completely destroy them, whereas a mixture of sulfoharnstoff and ascorbic acid destroyed both trypanosomes and spirochaetes. In the authors' opinion these observations furnish additional evidence that the activity or inactivity of a drug *in vitro* has nothing to do with its activity or inactivity *in vivo*.

W. Y.

FISCHL (Viktor) & FISCHL (Lili). Arzneifestigkeit, Avidität, Interferenz. [Drug-Resistance, Avidity and Interference.]-*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Sept. 18. Vol. 83. No. 3/4. pp. 324-335. [21 refs.]

This paper, which is of a rather technical nature, describes experiments dealing with the subject of drug-resistance.

It is recalled that SCHLOSSBERGER and MENK had recorded that a strain of nagana-Prowazek, which had been made resistant in mice to a trypanocidal gold derivative called "Sulfoharnstoff" proved to be sensitive to tartar emetic and trypaflavine, but definitely resistant to neosalvarsan and germanin; on the contrary, the same parent strain made resistant to neosalvarsan was found to be completely resistant to the arsenicals, somewhat resistant to tartar emetic, but normally sensitive to germanin and "Sulfoharnstoff."

The authors repeated this work with the same parent strain, but contrary to SCHLOSSBERGER and MENK found that the "Sulfoharnstoff" resistant strain was sensitive to neosalvarsan, trypaflavine and germanin. This "Sulfoharnstoff-fast" strain was then made resistant to trypaflavine. The sensitiveness of the strain to a large number of substances was then tested and the results given in a table. There follows a discussion of the significance of these results. It is especially difficult in drug-resistance experiments to understand why certain substances are almost always active (avid substances of EHRLICH), whilst other closely related derivatives exert no influence on the trypanosomes. Examples of such avid compounds are arsenophenylglycine, arsenophenoxy acetic acid and arsenophenylthioglycolic acid (EHRLICH) and the arsinic acid corresponding to arsenophenylglycine (YORKE and his collaborators). SCHNITZER recently has stated that myosalvarsan and solusalvarsan are avid compounds, but so far as myosalvarsan is concerned, this is not confirmed by the authors' experiments. As regards its avidity-index (SCHNITZER) or its resistant-factor (Fischl and SINGER) solusalvarsan stands midway between salvarsan and arsenophenylglycine.

The last portion of the paper is concerned with the chemotherapeutic interference phenomenon. It was found that ascorbic acid (Vitamin C) exercised a definite "interference" action against tartar emetic, arsenophenylglycine, m.amino-p-oxyphenyl-arsenoxide and trypaflavine. Details of the experiments are given in a table. W. Y.

VON JANCsó (Nikolaus) & VON JANCsó (Hertha). The Rôle of the Natural Defence Forces in the Evolution of the Drug-Resistance of Trypanosomes. I.—A Method for the Exclusion of the Natural Defence Mechanisms from Chemotherapeutic Processes.—*Ann. Trop. Med. & Parasit.* 1934. Oct. 19. Vol. 28. No. 3. pp. 419-438. [29 refs.]

The authors have devised a method which they claim enables them to exclude almost entirely the natural protective mechanism in rats and mice in trypanosome infections. The method consists essentially in splenectomy and in the intravenous injection of an electrically prepared colloidal copper solution.

This preparation was obtained from von Heyden and has 0.06 per cent. of copper content. Apparently the amount of copper, however, varies somewhat in different samples. With the latest solution supplied it was possible to produce a typical blockade by injecting 0.02 cc.

of the solution diluted with 4 times its volume of water, whereas with the earlier solutions a typical effect was only obtained if 0.05 to 0.1 cc. of the undiluted solution was injected. The well-tolerated dose must, therefore, be ascertained in the case of each solution injected.

It was found in mice so prepared that the red blood corpuscles of a chicken circulate in the blood for 24 to 36 hours, although in normal mice they have all disappeared in from 2 to 3 hours. The same holds true when *Sp. gallinarum* is injected. Not only the phagocytosis of trypanosomes, but the formation of trypanosomal antibodies is practically entirely excluded by this combined blockade. According to previous researches of the authors, the trypanocidal antibodies of the mouse are almost entirely formed in the spleen. This is proved by the facts that (a) infected splenectomized mice, which had been cured, exhibited no immunity against a second infection; and that (b) the trypanosomes appearing in the blood after the incomplete cure of splenectomized mice are sensitive to serum. Formation of serum-fast strains does not take place.

The authors' experiments indicate that humoral immunity plays an important part in the mechanism of cure, the specific antibodies killing off these trypanosomes which have escaped the chemotherapeutic shock. It follows from this that a definite cure may result even though the chemotherapeutic agent does not directly destroy all the trypanosomes in the body. The definite sterilization of the organism by minimal sterilizing doses of a drug is due in part to the intervention of immune bodies; and this accounts for the fact that when minimal doses of a drug are used splenectomy definitely interferes with the therapeutic effect. In such cases there is an early reappearance of the trypanosomes in the blood, even when the drug is given in doses which suffice to sterilize the normal animal.

The authors record some interesting observations on the mechanism of the action of germanin. They claim that the phagocytes of the reticulo-endothelial system play an important part in the curative mechanism, and that germanin exerts an opsonin-like action on the trypanosomes. As, however, after splenectomy and injection of the electro-colloidal copper solution, the natural mechanisms of defence are entirely excluded, owing to the poisonous effect of the colloidal copper solution on the reticulo-endothelial system, the phagocytosis of trypanosomes is abolished and trypanosomal immune bodies are produced only in traces.

W. Y.

WALLACE (J. M.). A Note on an Indirect Method of demonstrating Drug Resistance in Trypanosomes, *in vivo*.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 347-348.

The author points out that the disadvantage of the usual method of testing *in vivo* the resistance to arsenic of a strain of trypanosomes is the impossibility of giving a higher dose of the drug than is normally toxic to the host animal. In the experiments described in this paper guineapigs were treated with gradually increasing doses of trypanarsyl until they could withstand a dose which would be lethal if given as an initial dose. Twenty-four hours after the final dose of the drug "when the drug has had time to be absorbed from the peritoneal cavity," the animal is inoculated with the trypanosome believed to be resistant. The experiment, which is described in detail, was performed with the normal and resistant strains of *T. rhodesiense* sent to Uganda by the

reviewer. Wallace states that these experiments do not expose the trypanosomes to such a high concentration of drug as is possible *in vitro*, but that they enable the *in vivo* test to be extended, and they confirm existing views by indicating that drug-resistance is relative. [In the reviewer's opinion it will be necessary to know a good deal more about the fate, rate of excretion, etc., of a drug after its injection into the peritoneal cavity, before we are even justified in saying that this method of experimentation allows the *in vivo* test to be extended.]

W. Y.

- i. CULBERTSON (James T.) & STRONG (Paul S.). **The Trypanocidal Action of Normal Human Serum. The Nature of the Substance Responsible for the Trypanocidal Effect and its Relationship with the Bactericidal Activity of Normal Human Serum.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 1-17. [19 refs.]
- ii. HANDLER (Bernard J.). **Studies on the Trypanocidal Power of Normal Human Serum.**—*Ibid.* pp. 18-26. [14 refs.]

i. The authors have studied the nature of the substance responsible for the trypanocidal action of normal human serum, and particularly its relationship to alexin, firstly as regards the effect of heat upon each, secondly as regards their respective filtrability, and thirdly as regards their fixability by trypanosomes and other substances.

It was found that heating normal human serum sufficiently to inactivate alexin does not destroy the trypanocidal property, although this may be slightly reduced in potency. A serum of which the alexin is inactivated by heating is not re-activated in trypanocidal power by the addition of fresh guineapig serum potent in alexin. Repeated filtration of normal human serum through a Berkefeld filter enabled the trypanocidal substance to be separated from alexin, the latter being held up much more readily than the former. From various experiments it is concluded that the trypanocidal power of normal human serum is in its action independent of the several known components of alexin.

The trypanocidal property can be inactivated or absorbed from normal human serum by trypanosomes and certain bacteria, but not by charcoal or kaolin. Carmine inactivates both the trypanocidal and bactericidal substances in normal human serum; and experiments indicated that there is some degree of correlation between the bacteriocidal titre and the trypanocidal titre of normal human serum. The general conclusion is that the agent responsible for the trypanocidal activity of normal human serum is a relatively non-specific antibody, perhaps similar to the substance responsible for bactericidal activity.

ii. The work described in this paper was devised with the object of reinvestigating the observations upon which ROSENTHAL and FREUND described the "exhaustion phenomenon" [this *Bulletin*, Vol. 20, p. 700; Vol. 27, p. 238]. This phenomenon is broadly to the effect that repeated injections of human serum into mice rendered a subsequent therapeutic inoculation of the same agent ineffectual. ROSENTHAL and FREUND interpreted their experiments as indicating that some activating substance in the mouse had been exhausted, and hence that human serum is not trypanocidal, but trypanocidogenic.

The work of the reviewer and his colleagues had, however, shown that normal human serum exerted a direct lytic action on trypanosomes

in vitro. It was therefore with the object of clearing up these discrepancies that Handler undertook his present work. Experiments showed that human serum heated to 60°C. for one hour is just as effective as unheated serum in evoking the "exhaustion phenomenon" of ROSENTHAL and FREUND; this observation consequently failed to support the hypothesis advanced by these authors. Further experiment showed that the trypanocidal agent in normal human serum is capable of producing an equivalent antibody. When sufficient antiserum prepared against unheated human serum is added to normal human serum *in vitro*, neither the supernatant fluid nor the precipitate display any trypanocidal activity. But when antiserum prepared against heated human serum is used under similar conditions, the trypanocidal power of the supernatant fluid is not diminished. Similarly, the antagonistic effect *in vivo* could be elicited only with antiserum obtained by immunization with unheated human serum.

W. Y.

FUJIBAYASHI (Michizo). Studien ueber die trypanozide Kraft des Menschenserums. I. Ueber die trypanozide Kraft des Menschenserums und anderer Körpersäfte bei verschiedenen physiologischen und pathologischen Zuständen. II. Zusammenhang zwischen der trypanoziden Kraft des Menschenserums und der Blutplättchen. [I. The Trypanocidal Power of Human Serum and Other Body Fluids in Various Physiological and Pathological Conditions. II. The Relationship between the Trypanocidal Power of Human Serum and the Platelets.]—*Fukuoka Acta Med.* (*Fukuoka-Ikwad-aigaku-Zasshi*). 1934. Oct. Vol. 27. No. 10. [In Japanese pp. 2279–2308. [34 refs.]; pp. 2309–2364. [38 refs.] German summaries pp. 121–122; 122–123.]

I. The trypanocidal power of human serum is greatest in adult age; it may be increased or decreased by exercise. In cirrhosis of the liver and in cases of obstructive jaundice the trypanocidal power is either lost or at least decreased. It is also decreased in such diseases as Banti's, aplastic anaemia, secondary anaemia, haemophilia, myelogenous leukaemia and paroxysmal haemoglobinuria; but in typhoid, phthisis and acute and chronic infectious diseases it is almost normal. The author also examined the trypanocidal power of organ extracts and of the extracts which had been concentrated to $\frac{1}{10}$ of their original volumes by means of a vacuum. In cirrhosis of the liver, neither the original extract nor the concentrated form exhibited trypanocidal power. The cerebrospinal fluid of various patients showed no trypanocidal action even when concentrated.

II. In adult life and in old age there seems to be no relationship between trypanocidal power and the number of platelets, but in adolescence there is a tendency towards increase in platelets if the trypanocidal power is increased. In cirrhosis of the liver, both trypanocidal power and the number of platelets are decreased. The author tested in *in vitro* and in *in vivo* experiments the trypanocidal power of blood platelet extracts prepared in various ways; in 6 of 11 *in vitro* experiments and in 5 of 17 *in vivo* experiments a trypanocidal power was demonstrated. Finally, experiments were undertaken to ascertain whether the serum of rabbits immunized against normal human serum inhibited the trypanocidal power of human serum; the results were negative, but the serum of rabbits immunized against blood platelet

extract did inhibit the trypanocidal action of normal human serum. As the result of this work the author believes that the platelets play some part in the formation of the trypanocidal substance. W. Y.

POINDEXTER (Hildrus A.). **A Thermoprecipitation Reaction in *Trypanosoma equiperdum* Infection in Laboratory Animals.**—*Jl. Experim. Med.* 1934. Nov. 1. Vol. 60. No. 5. pp. 575-579. [11 refs.]

The work described in this paper was undertaken in order to ascertain whether *T. equiperdum* possesses a thermoprecipitinogen. Extracts of various organs and tissues of rats, guineapigs, and rabbits infected with *T. equiperdum* were tested by means of the precipitation reaction for the presence of a substance which reacts with the serum of recovered animals.

The extracts were prepared by cutting the organs into small pieces and triturating them in the presence of talc. To the triturate was added five parts of normal saline or water for each gram of the original organ. The suspension was then boiled for 5 minutes and allowed to cool. The liquid was separated by centrifugation. The extracts were generally prepared and used on the same day; 0.5 cc. of the clear extract was layered upon an equal quantity of immune serum in a small agglutination tube. The results were read after 30 minutes at room or body temperature, and again after 18 hours in the ice box. Experience showed that the most strongly positive reactions were obtained after a period of 18 hours in the ice box. As a result of this work, it was found that extracts of the spleen of rats, guineapigs and rabbits infected with *T. equiperdum* contained a thermoprecipitinogenic substance; this substance was not found within the body of the trypanosome itself. Antibodies to it were present in the serum of infected animals. Whilst the antibody seemed to be relatively less in the serum of rats than in other animals, the thermoprecipitinogenic power of extracts of the spleen of infected rats was equal to that of similar extracts of other animals. W. Y.

KUNERT (H.) & KRAUSE (M.). Nachtrag zur Arbeit: Findet in *Glossina morsitans* eine zyklische Entwicklung von *Trypanosoma evansi* statt? [Additional Note to the Authors' Paper on the Question of Cyclical Development of *T. evansi* in *Glossina morsitans*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Dec. Vol. 38. No. 12. p. 534.

In answer to various inquiries the authors give information regarding the age of the strain of *T. evansi* used in their earlier experiments on cyclical development [this *Bulletin*, Vol. 31, p. 597]. It was isolated from a camel about the middle of October, 1932, maintained in mice until the end of October and thereafter in guineapigs. At the date of the experiments in question (1933) the strain was therefore 8 months old. W. Y.

PERLA (David). **The Protective Action of Copper against *Trypanosoma equiperdum* Infection in Albino Rats.**—*Jl. Experim. Med.* 1934. Nov. 1. Vol. 60. No. 5. pp. 541-546.

In previous work [*ante*, p. 42] it had been shown that the addition to an adequate diet of small quantities of copper or iron, or both, during

a period of 10 days prior to infection with *T. lewisi* raised the natural resistance of the rat to the disease. In the present communication the effect of additions of copper salts to the diet on a subsequently induced infection with *T. equiperdum* was determined. It was found that copper, in amounts equivalent to 0.2 mgm. of elemental copper per rat per day, during a period of 10 days prior to infection with small numbers of trypanosomes, increased the natural resistance of the rat to the infection. The infection was aborted in all instances when the number of trypanosomes injected was 2,000, and in 75 per cent. of cases when the rats were injected with 10,000 trypanosomes. W. Y.

CORSON (J. F.). **The Action of "Bayer 205" on *Trypanosoma rhodesiense* in White Rats Infected by Tsetse-Flies.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 535–547. [22 refs.]

After giving a brief summary of previous experimental work on the prophylactic action of Bayer 205, Corson records certain observations made by himself. These, he states, are chiefly interesting because a recent strain of *T. rhodesiense* was used, transmitted by isolated infective laboratory-bred *G. morsitans*. The results are in general agreement with those of earlier work with old laboratory strains of trypanosomes, mechanically transmitted.

Details of the experiments are given in a series of tables. It was found that a dose of 0.015 gm. per kilo. of body weight did not protect white rats for 21 days against the bites of isolated tsetse flies infected with a recent strain of *T. rhodesiense*; and that a dose of 0.03 gm. per kilo. failed to protect for 40 days. In further experiments it was found that the restraining action of Bayer 205 on the development of trypanosomes was not seen in rats subinoculated from rats which had relapsed after treatment with this drug, nor in rats bitten by tsetses infected from treated rats during a relapse. W. Y.

DECOURSEY (Elbert). **The First Fatal Case of Chagas' Disease observed on the Isthmus of Panama.**—*Amer. J. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 33–40. With 3 figs.

This paper describes the findings at the autopsy on a black baby 3½ months old, which died at Land Lease in the Canal Zone. The history of the case is that the child became very weak after the first month; about 5 days before death there was fever, swelling of the face and extremities, and severe dyspnoea. On the last two days of life there was excessive vomiting and anuria.

The outstanding lesions were in the heart and in the brain. The entire myocardium contained an abundance of parasites and inflammatory cells. The lesions of the brain were quite different in that they appeared as inflammatory foci, which were fairly numerous, while the parasites were rare. The thyroid gland was unaffected, as were also the skeletal and unstriated muscles. W. Y.

DIAS (Emmanuel). **Persistence de l'infection par le *Schizotrypanum cruzi* chez l'homme. [Duration of the Infection of *T. cruzi* in Man.]**—*C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 506–507.

Details are given of a case in the blood of which *T. cruzi* was found, both by the method of inoculation of guinea-pigs and by the

xenodiagnostic method of BRUMPT, after the patient had been in the Oswaldo Cruz hospital at Rio de Janeiro for 12 years.

When she was admitted to hospital in 1922 she had a goitre with cretinism and pronounced mental changes. As she came from a *T. cruzi* infested district it was considered that she was probably suffering from Chagas' disease, an opinion which was confirmed by the fact that the serum gave a strongly positive Machado reaction. Many attempts to infect guineapigs by inoculation with the patient's blood failed, and it was not until 1934 that the blood was proved to contain trypanosomes. The author states that this case shows that *T. cruzi* can exist in the human body for many years.

W. Y.

CHAGAS (E.). Infection expérimentale de l'homme par le *Trypanosoma cruzi*. [Experimental Infection of Man with *T. cruzi*.]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 30. pp. 390-392. With 3 figs.

Further information is given regarding the patient experimentally infected with *T. cruzi* [ante, p. 37]. The patient died of cancer just over 6 months after inoculation with the trypanosome. Although the blood remained constantly infective for guineapigs, the patient presented few signs of the trypanosomal infection apart from certain electrocardiographic changes. At the post-mortem only the heart showed pathological changes due to the infection; and it was only in this organ that leishmania-forms were found. The predilection of *T. cruzi* for the myocardium is thus clearly indicated.

W. Y.

CHAGAS (Evandro). L'infection expérimentale chez l'homme par le *Schizotrypanum cruzi*. [Experimental Infection of Men with *T. cruzi*.]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 3. pp. 290-292.

In these experiments three patients suffering from incurable malignant disease were employed. The conclusion was reached that *T. cruzi* cannot pass through the unbroken skin, but that it readily traverses the intact conjunctiva.

The first experiment consisted in ascertaining whether *T. cruzi* from the faeces of a *Triatoma* infected from a human case would pass through the unbroken skin; and the second experiment was similar, except that the *Triatoma* was very heavily infected with a virulent strain of *T. cruzi* from an armadillo. Both were negative. In the third experiment material from the same source as used in the second experiment was deposited on the intact conjunctiva of a patient. Twelve days later there was a febrile disturbance accompanied by oedema of the eye. A guineapig inoculated with the blood two days later became infected.

W. Y.

WOOD (Fae Donat). Experimental Studies on *Trypanosoma cruzi* in California.—*Proc. Soc. Experim. Biol. & Med.* 1934. Oct. Vol. 32. No. 1. pp. 61-62.

Observations are described on *T. cruzi* isolated from *Triatoma protracta* in California. The faeces of 54 per cent. of *Triatoma* in San Diego County were infected, but nothing was found in the faeces of bugs collected in the vicinity of Berkeley and Los Angeles. Of 43 San Diego wood rats examined, one was found to be infected, thus incriminating

the animal as a reservoir host of *T. cruzi*. One hundred and thirty-four animals, belonging to 16 different species, were inoculated with the Californian strain of *T. cruzi*, and a list is given showing the number of each which became infected. Attempts made to intensify the infection by lowering the host's resistance by splenectomy, by injection of testicle extract, and by keeping the animals at a higher temperature, failed. Successive passages through different host species, covering a period of 103 days, indicated a stimulating effect upon the trypanosomes in that the incubation period progressively decreased from 35 to 20 days.

W. Y.

WOOD (Fae Donat). **Natural and Experimental Infection of *Triatoma protracta* Uhler and Mammals in California with American Human Trypanosomiasis.**—*Amer. Jl. Trop. Med.* 1934. Nov. Vol. 14. No. 6. pp. 497-517. With 24 figs. on 3 plates. [12 refs.]

The author states that for a period of four years he has been engaged upon the study of the life history of a trypanosome described in 1916 by KOFOID and MCCULLOCH from the digestive tract of *Triatoma protracta* found in nests of the San Diego wood rat. An extensive field of laboratory investigations has indicated that this parasite is a relatively non-virulent strain of *T. cruzi*.

The author summarizes the results of his work as follows :—

" 1. The blood-sucking bug, *Triatoma protracta* Uhler, and the wood rat, *Neotoma fuscipes macrotis* Thomas are natural carriers of *Trypanosoma cruzi* Chagas in Southern California.

" 2. The following animals have been experimentally infected with this trypanosome : albino rats, albino mice, rhesus monkeys, a puppy, an opossum (*Didelphis virginiana virginiana* Kerr), 2 species of dusky-footed wood rats (*Neotoma fuscipes annectens* Elliot and *N. f. macrotis* Thomas), and 5 species of white-footed mice (*Peromyscus eremicus fraterculus* [Miller], *P. californicus insignis* Rhoads, *P. californicus californicus* [Gambel], *P. maniculatus gambeli* [Baird], *P. truei gilberti* [Allen]).

" 3. The San Diego desert and southern parasitic mice and the Virginia opossum have all been found in wood rat nests in the infected locality, so it is possible that they, too, are carriers.

" 4. Leishmania bodies were seen in bone marrow, cardiac and voluntary muscle of infected animals.

" 5. Lesions composed of infiltration lymphocytes, monocytes, and plasma cells have been found in cardiac and voluntary muscles, cerebrum, and meninges.

" 6. Animals infected by this strain take light infections, showing few parasites or lesions and usually no symptoms.

" 7. Neither splenectomy, injection of testicle extract, nor increased temperature have any intensifying effect upon the infection.

" 8. Varying the host species gave progressively shorter incubation periods, indicating a stimulating effect upon the parasite.

" 9. One out of five attempts to reinfect animals succeeded, indicating a partial immunity.

" 10. This trypanosome has been cultured on semi-solid blood agar, the culture forms being comparable to the insect phase." W. Y.

DIAS (Emmanuel). Le xénodiagnostic appliqué à la trypanosomiase américaine. [**Xenodiagnosis in American Trypanosomiasis.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 3. pp. 287-289.

The author examined the blood (fresh and stained preparations) of over 100 inhabitants of Lassance, in the State of Minas Geraes, for

T. cruzi, and in a proportion of these cases the parasite was also sought by the xenodiagnostic method of Brumpt and by blood culture.

Most of the people examined lived in primitive huts of the kind favoured by *Triatoma*, which abounded. In all, the blood of 113 persons was examined microscopically; the results were negative: from 16 of these blood cultures were made, and here again the results were negative. The xenodiagnostic method was applied in 30 of the cases in whom blood examination had proved negative. For this work 3rd stage larvae and nymphs of laboratory-bred *Triatoma megista* were used. These insects had been fed only on clean guinea pigs before the experiment, and flagellates had never been found in such laboratory-bred *Triatoma*.

In all, 147 *Triatoma* fed on 38 persons, the number feeding on each varying from two to six. Between 41 and 51 days later the insects were dissected and five were found to be infected with *T. cruzi*. By this means two of the 38 persons were therefore discovered to be infected. Details of these cases are given. W. Y.

VILLELA (E.) & DIAS (Emmanuel). Sur la formation d'ulcérations chez les animaux infectés par le *Schizotrypanum cruzi*. [**Ulcerations in Animals infected with *T. cruzi*.**—*C. R. Soc. Biol.* 1934. Vol. 117. No. 30. pp. 394-396.]

A description is given of ulcerative lesions occurring spontaneously in dogs experimentally infected with *T. cruzi*. The ulcers may appear during the acute stage of the disease or later.

The lesions have the appearance of necrotic ulcers, circular in shape and with sharp margins; they are painful, develop rapidly, and penetrate deeply, sometimes reaching the bones or joints. Sections of deep lesions showed inflammatory foci, sometimes around the sebaceous follicles and at other times in the papillae of the dermis. The foci consist of endothelial cells or plasma cells or both; they are never formed by polymorphonuclear cells. Parasites were not found in the foci studied. In the sections of the open lesions (ulcers of the mouth, vagina and skin), foci containing parasites in greater or less numbers were found. These findings reminded Villela of the necrotic ulcerations he described in a human case of the disease in 1923; similar lesions have also been recorded in the naturally infected armadillo. These facts indicated once again the biological affinities of *T. cruzi* with the genus *Leishmania*. W. Y.

VILLELA (Eurico) & DIAS (Emmanuel). Localisation des formes de multiplication du *Schizotrypanum cruzi* dans la peau et dans les muqueuses de chiens expérimentalement infectés. Parasitisme de la cellule épithéliale de l'épiderme. [**Localization of Multiplication Forms of *T. cruzi* in the Skin and Mucous Membranes of Experimentally Infected Dogs.**—*C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 501-504. With 3 figs.]

Further details are given of the localization of the parasites in the cellular elements of the skin and intestinal mucous membrane of dogs infected with an armadillo strain of *T. cruzi*.

As mentioned in their previous paper, this strain frequently produced cutaneous ulcerations. In certain cases sections of the cutaneous ulcers showed an intense parasitism of the lesions. As usual the leishmania

forms were found in great number in the histiocytes of the cutaneous tissue. The elements situated in the vicinity of the hair follicles and sebaceous glands were chiefly involved; they presented at the periphery a more or less intense reaction characterized by an infiltration of mononuclear cells, plasma cells, and in the ulcerated regions by an agglomeration of polymorphonuclear cells and a deposit of fibrin and the formation of a micro-abscess. ADLER and others have drawn attention to the similar localization of *Leishmania canis* in the vicinity of hair follicles and sebaceous glands.

The most remarkable fact observed by the authors was the presence of parasitized cells in the epidermis. Parasites were also found in the gastro-intestinal submucosa. In the stomach of one dog a large focus of infected cells was found which extended up to the muscularis mucosae close to the epithelium.

W. Y.

TANGANYIKA TERRITORY. A Further Account of the Anti-Tsetse Campaign in Tanganyika Territory by Officers of the Tsetse Research Department.—Reprinted from *Tanganyika Standard* between Oct. 17, 1933 and May 1, 1934. 32 pp.

To the intelligent layman wishing to know what the Tsetse Research Department in Tanganyika Territory has done and is doing, this interesting pamphlet should convey much useful and reassuring information. The scope of the publication is sufficiently indicated by the following chapter-headings: "Driving the Tsetse by Fire"; "Anti-Tsetse Clearings by Tribal Labour"; "Advances of Tsetse Fly"; "The Provision of Water in Reclaimed Country"; "Wresting Large Areas of Grazing from the Tsetse"; "Experiments in the Elimination of the Tsetse Fly by Means of 'Faunal' Control"; "Elimination of the Tsetse Fly by Means of 'Floral' Control"; and "A Concluding Survey of our Tsetse-Flies and of the Present Prospects of Controlling Them."

Of the seven species of tsetse in Tanganyika Territory, by far the most important are *Glossina morsitans*, *G. swynnertoni* and *G. pallidipes*, and the majority of the fly-belts are either "spreading or nearly stationary"; spreading is believed to be reconquest of territory occupied by the insect perhaps before the appearance of man. In Shinyanga, as a result of measures carried out under the auspices of the Tsetse Research Department, the fly has been not only stopped but driven back, and 30,000 people, previously forced to abandon their homes, are now gradually returning.

Facts and arguments on both sides in the perennial "tsetse-fly—big game" controversy are impartially presented, and, on behalf of the game, it is concluded that "if the game is so reduced that the fly-population [*G. morsitans* group] becomes hungry, wide spread may be expected." The special merits of "floral" or "vegetational" control, *i.e.*, the *alteration* instead of destruction of the plant-communities which shelter the fly, are explained, and this method of attack is considered to be "perhaps the most promising of all." E. E. Austen.

LEWIS (E. Aneurin). Tsetse-Flies in the Masai Reserve, Kenya Colony.
—*Bull. Entom. Res.* 1934. Dec. Vol. 25. Pt. 4. pp. 439-455.
With 1 folding map.

The Masai Reserve lies on the Tanganyika border and comprises some 10,000,000 acres, of which about 800,000, though of pasturage,

are infested by tsetse-flies and therefore useless. Extending "from about 34° 37' to 38° 15' E. Long. ; and from about 0° 34' to 3° 10' S. Lat.", the Reserve, described in some detail in the first part of this paper, includes a wide variety of country, altitude and vegetation. Within the Reserve six species of *Glossina* (*G. brevipalpis*, *G. fuscipleuris*, *G. longipennis*, *G. pallidipes*, *G. palpalis* and *G. swynnertoni*) are found, and notes are given on the local occurrence of each of these. The presence of *G. swynnertoni*, a vector of human as well as animal trypanosomiasis, hitherto believed to be confined to the Mwanza district of Tanganyika, may well prove to be a matter of some importance, since Osero, a district of about 700 square miles forming the south-western region of the Reserve, is believed to be "completely infested" with this fly, as well as with *G. pallidipes*.

It would seem that, since the institution of the present Masai Reserve, the fly-belts within its confines have extended their boundaries and increased in number ; and in the case of *G. swynnertoni* available evidence tends to show that there has been an actual invasion from Tanganyika Territory. The readiness with which *G. swynnertoni* attacks man in the presence of cattle, but where game is scarce, has previously been recorded by SWYNNERTON ; in the Masai Reserve the present author found that :—"In the presence of an abundance of game and in the absence of cattle . . . *G. swynnertoni* very readily approached man and was attracted to moving vehicles such as cars and lorries."

While tsetse-fly infestation of the Masai Reserve is serious, the customs and traditions of the people in relation to manual labour are likely to militate against the possibility of reclaiming the known infested areas. E. E. A.

JACKSON (C. H. N.). **A Note on the Concentrations of Tsetse-Flies.**—*Bull. Entom. Res.* 1934. Dec. Vol. 25. Pt. 4. pp. 457-458.

During the dry season in Tanganyika *Glossina morsitans* increases in numbers in actual vleis or drainage valleys, "as distinct from the bordering woodland." Observations by BURTT at a waterhole in a drainage valley or narrow vlei, after the beginning of August, support the author's contention that "the increase of fly in the vlei in the hot, dry months is due, not to a search for better shade conditions, but to the fact that the vlei is a feeding-ground, and that the fly must visit it more frequently at the season when . . . the onset of hunger is hastened by hot, dry conditions." E. E. A.

SWYNNERTON (C. F. M.). **Protection of Vegetation against Grass-Fires as a Possible Solution for Some Tsetse Problems.**—*Bull. Entom. Res.* 1934. Sept. Vo. 25. Pt. 3. pp. 415-430. With 1 plan, 1 folding chart, & 12 figs. on 4 plates. [12 refs.]

In Tanganyika Territory, to which this paper refers, it was found in 1925 "that even the relatively low deciduous thicket of the Central Province . . . tended strongly to exclude *Glossina morsitans*." It was thereupon decided "to test the possibility of reproducing these inimical conditions (a) by advancing the natural vegetational succession by not burning the grass, (b) by cheap or remunerative planting." The results of experiments on *G. swynnertoni* and *G. pallidipes* at Shinyanga in pursuance of this policy are here described. Although the cessation of annual burning of vegetation has had little effect upon the game,

certain sections of road on which tsetse were formerly "a serious nuisance" are, now that they are protected by thicket barriers, relatively free from fly. Barriers of deciduous thicket, impassable to fly in the wet season, may be so contrived as to restrict tsetse to areas insufficient for their needs. Yet the effects of not burning will differ with the species of tsetse concerned. "*G. morsitans* can exist under more humid conditions than does *G. swynnertoni*." *G. brevipalpis*—not perhaps of great practical importance—is, owing to the nature of its normal habitat, more likely to be assisted than otherwise by the cessation of annual fires. It remains to be proved whether the more dangerous *G. pallidipes*, which in Tanganyika occurs throughout more than half the area occupied by *G. morsitans* and *G. swynnertoni*, will be helped or hindered.

In selected sites, carefully controlled experiments are to be made in connection with game, by means of which it is hoped to discover whether the fly is specially dependent upon particular species; whether the fly can be abolished by "anything short of the complete extermination or expulsion of animals"; and "whether such extermination (locally) is practicable by such means as are cheaply available to a government."

Pending the final results of investigations as yet unfinished, the author is inclined "to regard the release of the vegetational succession by the prevention of grass-burning as likely to be useful as a *basic* measure," to be supplemented or replaced by others as and where required.

E. E. A.

HENRARD (C.). Quelques essais de capture de *Glossina palpalis* au moyen de divers types de piège Harris près du Stanley pool. [*Trials of Various Types of Harris Trap for the Capture of *G. palpalis* near Stanley Pool.*—*Ann. Soc. Belge de Méd. Trop* 1934. Sept. 30 Vol. 14. No. 3. pp. 263–276. With 2 figs.]

The tests described were carried out between October 1933 and February 1934, on an island in the Congo west of Leopoldville, whereon wild animals were present in limited numbers, while crocodiles were numerous in the vicinity. The greatest average density of *G. palpalis* where the fly was most numerous was from 10 to 15 per fly-boy hour. Four traps were used, and of these the most efficient was one capable of being taken to pieces, and when in use suspended from a branch. While the average number of tsetse caught per trap during a month of fine weather was 2,000, the monthly figure for the whole period was only 850.

Traps were found to yield the best results when men or animals were present or passed by [*cf.* SWYNNERTON on the value of animal scent, this *Bulletin*, Vol. 30. p. 618]. The author's final conclusion is that Harris traps, appropriately sited, can usefully be employed for the local protection of human beings and domestic animals.

E. E. A.

BUXTON (P. A.) & LEWIS (D. J.). *Climate and Tsetse Flies: Laboratory Studies upon *Glossina submorsitans* and *tachinoides*.*—Reprinted from *Phil. Trans. Roy. Soc. London*. Ser. B. 1934. Dec. 14. Vol. 224. No. 512. pp. 175–240. With 14 text figs. & 5 figs. on 2 plates. [38 refs.]

Previous workers have studied the effects of climate upon wild populations of *Glossina*, and have obtained valuable results. The

authors of this paper have worked in the laboratory, and have attempted to analyse the effects of controlled conditions of temperature and humidity. Many suggestive results were obtained, which should greatly encourage further work of this sort. The work was done in the laboratory of the Tsetse Investigation at Gadau in Northern Nigeria.

The upper and lower limits of temperature at which the adult flies could survive were found, and the effects of humidity on the thermal death points were investigated. The time which adults could survive each controlled condition was determined, in some experiments using starved individuals and in others giving the flies opportunities of feeding daily. The rate of reproduction under these conditions was also studied. The rate of loss of water and of fat metabolism was found. Experiments were also made with puparia. Finally, continuous records of temperature and humidity were made both in an open clearing and in a dense thicket, in dry and wet seasons.

While the effects of temperature appear to be simple—there is a fairly narrow zone within which the fly can live satisfactorily—the effects of humidity are more complex. With a temperature of 30°C., a relative humidity of about 44 per cent. appears to be near the optimum at which the flies live longer and breed more rapidly than in drier or in moister air. A relative humidity of only 65 per cent. was unfavourable, and in moister air the flies died off very rapidly, and fed with reluctance. The reason why high humidities are unfavourable is still obscure.

At temperatures above 40°C. the adult flies survive better in dry air than in moist. They also metabolized fat most rapidly in dry air, presumably to produce metabolic water to compensate for excessive evaporation.

The puparium was shown to have an optimum humidity near saturation, and it is suggested that the air in the spaces in apparently powder-dry soil may be much moister than is usually imagined, even when the general atmosphere is very dry. Unfortunately the soil conditions were not investigated further.

The field meteorological results support the laboratory work most satisfactorily. When the humidity was high, the flies were scarce, and many workers have found that pregnancies are rare under these conditions.

Various practical measures of control, such as clearing of undergrowth, are discussed in the light of the experimental results.

K. Mellanby.

DE LA CAMARA (Pedro). Accion de algunos arsenicales organicos sobre la morfologia de los tripanosomas.—*Medicina Paises Calidos*. Madrid. 1934. Oct. Vol. 7. No. 10. pp. 460-469. With 2 figs. & 1 coloured plate. English summary (8 lines).

GEOGHEGAN (Arnoldo J.). Nuevo caso de tripanosomosis humana en la ciudad de Catamarca.—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Mar. Vol. 6. No. 2. pp. 212-215. With 2 figs.

GEOGHEGAN (Arnoldo J.). Nuevo caso de tripanosomosis humana en Huillapima (Catamarca).—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Mar. Vol. 6. No. 2. pp. 216-219. With 3 figs.

- MAZZA** (Salvador) ; **CORNEJO** (Andrés). Casos agudos benignos de enfermedad de Chagas comprobados en la Provincia de Jujuy.—*Rev. Med.-Cirurg. do Brasil*. 1934. Sept.-Oct. Vol. 42. Nos. 9-10. pp. 308-316.
- ROMAÑA** (Cecilio). Novas investigações sobre a molestia de Chagas na Republica Argentina.—*Rev. Med.-Cirurg. do Brasil*. 1934. Sept.-Oct. Vol. 42. Nos. 9-10. pp. 298-307.
- TORREALBA** (J. F.). El primer caso de tripanosomosis americana diagnosticado en el estado Guárico por el exámen directo de la sangre.—*Gac. Med. de Caracas*. 1934. Sept. 30. Vol. 41. No. 18. pp. 275-279. [16 refs.]
- UNIVERSIDAD BUENOS AIRES MISIÓN DE ESTUDIOS DE PATALOGÍA REGIONAL ARGENTINA JUJUY**. 1934. Publicación No. 18. 32 pp. With 25 figs. Investigaciones sobre la enfermedad de Chagas. I. Casos crónicos de enfermedad de Chagas determinados en Jujuy [Mazza (Salvador)]. II. Casos crónicos de enfermedad de Chagas, demostrados en Salta [Mazza (Salvador) & CORNEJO (Andrés)].
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VENOMOUS SNAKES AND SNAKE VENOMS. II.*

Not many new data have been published in regard to geographical distribution of the Ophidia. PHISALIX and HOUEMER¹ report on the venomous snakes of Indo-China. Of the proteroglyphous colubrids both the Hydrophinae and Elapinae are represented. The sea snakes observed on the Indo-China coast include species of the genera *Platurus*, *Hydrophis*, *Distira*, *Hydrus*, *Enhydris* and *Enhydrina*, the venom of the latter being ten times as toxic as cobra venom. The elapines include four genera, *Callophis*, *Doliophis*, *Bungarus* and *Naja*; the most common species are *Bungarus fasciatus*, *Naja tripudians* and *Naja bungarus*. The crotaline vipers are represented by species of the genera *Ancistron* and *Lachesis*.

I. Ophidian Dentition and Evolution of the Poison Fang.

SMITH² introducing this subject at the Royal Society of Medicine pointed out that snakes had originally been derived from lizards or some lizard-like creature, and that most of the primitive snakes still showed some evidence of their four-footed ancestry, notably by the presence of a pelvis and vestiges of hind limbs. From one of these primitive groups the family Colubridae had been formed, and it was from the Colubridae that the poisonous snake had been derived. The Colubridae were a large family and capable of division in terms of their dentition into the Aglypha with solid non-grooved teeth, the Ophisthoglypha which have grooved teeth or fangs at the back of the mouth, and the Proteroglypha, which have tubular or canalized anteriorly-situated fangs. The Ophisthoglypha had been derived from the Aglypha and both have in their turn given rise to the Proteroglypha. The venomous snakes were late arrivals upon the earth and represented a high degree of specialization in which the evolution of the poison fang was secondary to the salivary venom gland. Actually the back-fanged snakes were only rarely venomous to man, the vast majority being quite harmless. The front-fanged snakes on the other hand—the Proteroglypha—were highly toxic; they could be divided into two groups having divergent lines of evolution—the Elapidæ and the Viperidæ.

In the Elapidæ the poison fangs were comparatively short and the maxillary bone long, having behind one to eighteen smaller grooved teeth; not infrequently the teeth upon the palatine and dentary bones were more or less distinctly grooved, but never tubular. The normal position of the elapine fang was almost vertical in the mouth, approximately at right angles to the maxillary bone.

In the Viperidæ the maxillary bone, which was very short and bore the fangs only, was moveably attached to the prefrontal and the ectopterygoid so that during striking the bone and the fang upon it could be erected. The resting position of the viperine fang was almost horizontal in the mouth, and the ability to fold these greatly elongated fangs back had become imperative for the preservation of the species.

*For the first of this series see Vol. 31, p. 99.

¹ PHISALIX & HOUEMER (E.). Contribution à la faune venimeuse du Tonkin.—*Bull. Soc. Path. Exot.* 1934. Feb. 14. Vol. 27. No. 2. pp. 178-184.

² SMITH (Malcolm A.). The Classification of Snakes in Accordance with their Dentition and the Evolution of the Poison Fang.—*Proc. Roy. Soc. Med.* 1934. June. Vol. 27. No. 8. pp. 1081-1083 (Sec. Trop. Dis. & Parasit. pp. 43-45).

Nothing was known concerning the evolution of the poison fang in the clarine snakes ; no non-venomous snakes with grooved anterior teeth have been encountered, while the initial stages which have led to the formation of the elapine type of fang have not yet been found. The vipers, on the other hand, have obviously been derived from the Ophisthoglyphous snakes by the gradual movement forward and shortening of the maxillary bone ; as this bone became progressively shorter more and more teeth on its anterior part were lost until finally a stage was reached when only the posterior fangs remained ; these would now be located in the front of the mouth. One could arrange amongst the Ophisthoglypha a complete series showing this gradual shortening of the maxillary bone starting with *Oxybelis*, which has twenty or more teeth in front of the fangs, and culminating in *Miodon* which has only two. The ability to erect or depress the fangs became developed as the maxillary bone grew shorter and *Xenodon*, one of the Aglyphous snakes, actually could move its maxillary bone like the vipers. The power to erect in some degree the maxillary bone was widely spread among the Proteroglypha and in fact was only a further development of the power to move the jaw independently which all snakes possess.

II. *The Mechanism of Bite.*

FAIRLEY³ at the same meeting dealt with methods of taking dental impressions of the bite and the significance of the " maxillary index " and the " quadrate index " which he had introduced for determining the biting efficiency of the Australian colubrids. In snake bite four distinct phases were recognized : (1) the strike ; (2) opening the mouth and elevation of the fangs ; (3) closing the mouth and the injection of venom ; (4) retraction of the fangs. In the Australian colubrids there was a wide range of variation in the mobility of the fangs, the degree of elevation from extreme retraction to maximal protraction varying from 10°-15° to 45°-50° in the different species studied. Each pterygo-palatine-transverse arch acted as a single entity, and when the protractor muscles of the palate drew the endo-pterygoid forward, they invariably brought with it the palatine bone and the ecto-pterygoid which impinged on the posterior arm of the maxilla, driving the maxilla forwards and upwards on the articulating surface of the prefrontal. This produced a variable degree of elevation and forward rotation of the fangs which were ankylosed to the inferior surface of the maxilla ; its extent could be judged by the angle formed at the ecto-pterygoid maxillary junction which, in the resting position, formed a straight line. Should this movement be doubted it could readily be demonstrated by pithing the snake, dissecting up the mucous membrane on the roof of the mouth and electrically stimulating the protractor and retractor muscles acting on the palatine arch ; alternatively, skulls could be prepared with the palatine arch in different positions. In these snakes the smaller the maxilla (*i.e.*, the greater the maxillary index), the greater the forward movement of the pterygo-palatine-transverse arch and the greater the degree of forward projection of the fangs. This mechanism differed from that of the vipers, in which the movement of the maxilla on the prefrontal was a true rotary one and not a forward and upward sliding movement as described above.

³ FAIRLEY (N. Hamilton). Snake Bite : its Mechanism and Modern Treatment. —*Proc. Roy. Soc. Med.* 1934. June. Vol. 27. No. 8. pp. 1083-1091 (Sec. Trop. Dis. & Parasit. pp. 45-53). [23 refs.]

III. Venom Yields.

FREEMAN and KELLAWAY⁴ report on the venom yields obtained by milking the common Australian snakes over a period of several years. For the tiger snake (*Notechis scutatus*) the average yield for 3,214 milkings equalled 0.0276 grams of dry venom, and for the black tiger snake (*Notechis scutatus* var. *Niger*) the average of 516 milkings was 0.07 grams. For the death adder (*Acanthophis antarcticus*) 926 milkings from 360 snakes showed an average yield of 0.04 grams, while for the copperhead (*Denisonia superba*) the average of 1,940 milkings equalled 0.0215 grams. The latter species does not thrive well in captivity and the primary are considerably larger than the secondary yields: they were found to do better if milked at 6 instead of 3 weeks' interval. The average yield of 579 milkings from 170 black snakes (*Pseudechis porphyriacus*) was 0.03 grams: they seldom survived longer than 7 to 8 months. Fifty brown snakes (*Demansia textilis*) were under observation and these did least well in captivity; the average yield of 126 milkings was only 0.002 grams; this, however, does not represent the venom injected at a single bite in nature, as one brown snake measuring nearly 7 feet in length yielded 0.045 grams at a first bite, and an addition 0.0222 grams on milking.

IV. Bacterial Flora of Snakes' Mouths.

WILLIAMS, FREEMAN and KENNEDY⁵ investigated this question in captive Australian snakes. They found that freshly caught snakes did not possess a very numerous oral bacterial flora, but in captivity the number of organisms present in their mouths multiplied enormously and included anaerobes, non-lactose-fermenters, coliform bacilli and staphylococci. Freshly collected venom contained many fewer organisms and about 30 per cent. of samples were sterile, those infected containing only one or two species of organism. Over 50 per cent. of the samples of adequately dried venom were sterile, the drying apparently killing off many of the non-lactose-fermenters. The ordinary methods of collection and handling of venom, though they excluded gross contamination by saliva, did not guarantee sterile dry venoms. Measures for the exclusion of laboratory contamination of the venom are described. "Cancre" in captive snakes was frequently found to be associated with a strain of *Proteus* or with a small Gram-negative coccus-bacillus.

V. Some Rarer Australian Snakes and their Venoms.

KELLAWAY^{6, 7, 8}, in a series of papers reports investigations on some of the rarer Australian snakes and their venoms, including *Denisonia*

⁴ FREEMAN (Mavis) & KELLAWAY (C. H.). The Venom Yields of Common Australian Poisonous Snakes in Captivity.—*Med. Jl. Australia*. 1934. Sept. 22. 21st Year. Vol. 2. No. 12. pp. 373-377.

⁵ WILLIAMS (F. Eleanor), FREEMAN (Mavis) & KENNEDY (Eileen). The Bacterial Flora of the Mouths of Australian Venomous Snakes in Captivity.—*Med. Jl. Australia*. 1934. Aug. 11. 21st Year. Vol. 2. No. 6. pp. 190-193.

⁶ KELLAWAY (C. H.). The Venom of the Ornamented Snake *Denisonia maculata*.—*Australian Jl. Experim. Biol. & Med. Sci.* 1934. June 16. Vol. 12. Pt. 2. pp. 47-54. With 2 figs.

⁷ KELLAWAY (C. H.). The Venoms of Some of the Small and Rare Australian Venomous Snakes.—*Med. Jl. Australia*. 1934. July 21. 21st Year. Vol. 2. No. 3. pp. 74-78. With 1 fig.

⁸ KELLAWAY (C. H.). The Venoms of the Broad-Headed Snake (*Hoplocephalus bungaroides*) and of the Yellow-Banded Snake (*Hoplocephalus stephensi*).—*Med. Jl. Australia*. 1934. Aug. 25. 21st Year. Vol. 2. No. 8. pp. 249-255. With 1 fig.

maculata var. *devisii* (South-Western Queensland). A bite in man by this snake was followed after an interval by sudden loss of consciousness, from which recovery occurred some few hours later with dramatic suddenness. A somewhat similar phenomenon was observed in rabbits injected intravenously with sub-lethal doses of venom. The venom itself appeared rather less potent than that of the copper-head both in respect of its haemolytic and neurotoxic properties, and had a strong paralysing action—which was spontaneously reversible—on the phrenic motor endings in the diaphragm.

Four other small species of *Denisonia* were studied, *D. daemeli* Günther, *D. flagellum* McCoy (the little whip snake), *D. suta* Peters and *D. coronoides* Günther (the white-lipped snake); their venom in all instances was similar to the common copper-head, *Denisonia superba*, but, unlike it, none was dangerous to man or large animals. The venom of *Demansia olivacea* Gray, apart from the possession of feeble thrombin, bore very little resemblance to the highly potent venom of *Demansia textilis*, while that of *Demansia psammophis* Schlegel was not highly toxic either. The venom of the *Furina annulata* Dumeril contained no coagulent principle and was not highly poisonous. None of these snakes was dangerous to man and their slender build went hand in hand with narrow heads, small venom glands and small venom yields, a correlation originally described by FAIRLEY and SPLATT when studying the larger and commoner Australian snakes.

Of the three species of the genus *Hoplocephalus*, no specimens of *H. bitorquatus* Jan were available; according to KINGHORN this snake is venomous, but not deadly. The broad-headed snake, *H. bungaroides* Boie, is an aggressive snake attaining 5 feet in length and must be regarded as definitely dangerous. Its broad head also suggests a large venom yield, though no information on this point is available. Its venom, judged by injection in three species of animals, is of about the same order of toxicity as that of the copper-head and resembles the tiger snake in possessing a powerful thrombin, only a feeble haemolytic action and inducing peripheral paralysis causing death by respiratory failure; its local action is more severe than any other of these venoms. As it is a rare snake KELLAWAY tested the neutralizing effects of tiger snake antivenenes on the venom of *H. bungaroides* and found very effective protection; its use is therefore advocated clinically.

A single specimen of the yellow-banded snake, *H. stephensi*, was studied in captivity for 3 months: its venom was found to resemble *H. bungaroides*, but the relatively small size of its venom yield makes it unlikely ever to prove fatal to man.

VI. Toxicity of the Crotaline Venoms of Formosa.

KYU⁹, who previously has published data on the toxicity of the venom of *Trimeresurus gramineus* Shaw, and *T. mucrosquamatus* Cantor, now reports on that of *Ancistron acutus* Günther, for frogs, mice and rabbits. The potency of the venoms was in the above order and did not correspond to the human mortality figures from snake bite, which were *T. gramineus* (1 per cent.), *T. mucrosquamatus* (9 per cent.),

⁹ KYU (Kenten). Toxikologische Untersuchungen ueber die Gifte der Crotalinae Formosa's. III. Mitteilung. Studien ueber das Gift von *Aghistrodon acutus*, Günther.—*Taiwan Igakkai Zasshi* (Jl. Med. Assoc. Formosa). 1933. Nov. Vol. 32. No. 11 (344). [In Japanese pp. 1500–1522. With 7 figs. German summary pp. 148–151.]

and *A. acutus* (23 per cent.). The anomaly is explained on the basis of the different amounts of venom secreted for the three species. SUZUKI, MATSUMOTO and SUGIO¹⁰ determined the minimum lethal dose of the above Formosan venoms for the mongoose as well as for *Bungarus multicinctus* and *Naja naja atra*, and compared the relative resistance of the mongoose, rabbit and guineapig. The mongoose was far more resistant to the venoms of *Naja naja atra* and *Bungarus multicinctus* than to the others. The serum of the mongoose was found to neutralize *Naja* venom, but not that of the other snakes, and this power was considerably diminished by heating to 56°C. for 15 minutes and lost after 30 minutes at that temperature. The red corpuscles of the mongoose could also neutralize *Naja* venom, a power not possessed by the leucocytes.

VII. Pharmacological and other Observations on Snake Venoms.

VELLARD and VIANNA¹¹ group the actions of various venoms into (1) neurotropic including the curari and hypotensive effects; (2) action on phosphatids which play a part in haemolysis, coagulation and cytotoxicity; (3) action on proteids destroying fibrinogen and complement and causing local oedema, haemorrhages and gangrene; (4) coagulant action, transforming prothrombin into thrombin, while others act on the plasma. Observations both *in vitro* and *in vivo* were made on *Lachesis*, *Crotalus terrificus*, *Naja* and *Elaps*; the conclusion reached was that as regards their biological actions two types of snake venom exist—Colubrine and Crotaline. The Colubrine type, seen in *Elaps* and *Naja*, acts almost exclusively on the phosphatids and to a much less degree on the proteids. Both have a definite neurotropic action, but differing in the way in which this is exerted. The Crotaline type (*Lachesis* and American *Crotalus*) in addition to a marked action on phosphatids acts powerfully on proteids. *C. terrificus* has marked coagulant effects on proteids, bringing about the disappearance of fibrinogen, but not destroying proteids altogether. The differences in proteolytic effects between *Lachesis* and *C. terrificus* are quantitative rather than qualitative, the former being stronger. The *C. terrificus* of the North has a much more powerful proteolytic venom than that of the South, while all the Crotalines of Central and North America have venoms more potent in this respect than *Lachesis*.

The Anti-Complementary Action of Different Venoms.—VELLARD and VIANNA¹² find that the venoms of the genera *Lachesis* and *Tremesurus* are anti-complementary, but that their activity in this respect varies with different species. The venom of *Naja tripudians* is much less active, while those of *Crotalus terrificus* and of *Vipera aspis* are not found under experimental conditions to have any action on complement. Considerable differences were observed between the venoms of different species of *Lachesis* and *Crotalus*, and perceptible differences existed between different geographical varieties of *Lachesis newwiedii*,

¹⁰ SUZUKI (Ch.), MATSUMOTO (K.) & SUGIO (K.). Ueber die Widerstandsfähigkeit der Manguste gegen Schlangengift.—*Taiwan Igakkai Zasshi* (Jl. Med. Assoc. Formosa). 1934. Feb. Vol. 33. No. 2 (347). [In Japanese pp. 305-314. With 1 fig. German summary pp. 24-25.]

¹¹ VELLARD (J. A.) & VIANNA (M. Miguelote). Acção comparada dos diversos venenos ophidicos.—*Rev. Med.-Cirurg. do Brasil*. 1934. Feb. Vol. 42. No. 2. pp. 59-67.

¹² VELLARD (J. A.) & VIANNA (Miguelote). Complemento e venenos ophidicos.—*Rev. Med. Cirurg. do Brasil*. 1933. Oct. Vol. 41. No. 10. pp. 289-322. [11 refs.] French summary.

though they are little marked in those of *Lachesis jararaca* and *Crotalus terrificus*. A certain incubation period is necessary for the action of venom on complement which varies from 15 minutes to 2 hours; some venoms act rapidly, others slowly.

The properties of the venom are not modified after exerting its anti-complementary action, which is due to its proteolytic effect and not to its coagulant properties. Thus the venom of *Naja* is strongly anti-coagulant and non-proteolytic and shows slight anti-complementary tendency; the venom of *V. aspis* only acts on certain albuminoids and does not affect complement at all.

Enzymes in Venom.—DUNN¹³ has studied the action of the enzymes of the venom of *Crotalus adamanteus* on the proteins of blood and milk and found that they were all digested.

One or more proteolytic enzymes were present which digested plasma and serum proteins, and with less rapidly serum albumen and globulin; there was also a weak but definite action on rennin. *Crotalus* venom was found to transform haemoglobin into methaemoglobin in solution, but with non-haemolysed corpuscles methaemoglobin could be detected only after slight haemolysis had occurred.

In another paper DUNN¹⁴ reports having separated the enzymes and toxic principles of the venom of *Crotalus adamanteus*. Its ability to destroy cephalin and to digest protein were found to be due to separate constituents. An albumose fraction was prepared which contained cephalinase, but was free from proteolytic activity; a portion of the toxicity of the venom was contained in this fraction which had haemolytic powers of the same order as the original venom. The toxic principles, enzymes and proteins of the venom are all adsorbed by freshly prepared aluminium hydroxide C, while the substance which oxidizes haemoglobin to methaemoglobin is different from proteinase and cephalinase and is easily separated from them.

The Central and Peripheral Action of Snake Venoms.—KELLAWAY¹⁵ continued his studies on the peripheral action of Australian snake venom with special reference to the sensory nerve endings in frogs. The Australian venoms studied were derived from the black snake, the copper-head, the death adder, the tiger snake and the black tiger snake; that of the Indian cobra was also included. All the venoms were found to have a paralysant action *in vitro* on sensory nerve endings in *Hyla aurea*, though this was less powerful than their action upon the motor endings in this species. The arrangement of the venoms in the order of potency was the same for both sensory and motor nerve endings. Curari also paralyses sensory endings *in vitro*, but this action is overshadowed by its much more powerful effect on motor endings.

¹³ DUNN (Edwin E.). The Action of the Enzymes of the Venom of *Crotalus adamanteus* on the Proteins of Blood and Milk.—*Jl. Pharm. & Experim. Therap.* 1934. Apr. Vol. 50. No. 4. pp. 386-392. [12 refs.]

¹⁴ DUNN (Edwin E.). The Separation of the Enzymes and Toxic Principles of the Venom of *Crotalus adamanteus*.—*Jl. Pharm. & Experim. Therap.* 1934. Apr. Vol. 50. No. 4. pp. 393-406. [22 refs.]

¹⁵ KELLAWAY (C. H.). The Peripheral Action of Australian Snake Venoms. 4. Action on Sensory Nerve Endings in Frogs.—*Australian Jl. Experim. Biol. & Med. Sci.* 1934. Dec. 16. Vol. 12. Pt. 4. pp. 177-186. With 3 figs.

VENKATACHLAM and RATNAGIRISWARAN¹⁶ report some experimental observations on the venom of the Indian cobra, and reopen the question whether the respiratory paralysis so produced is due to central or peripheral action. They found that while sub-lethal doses of the venom, so regulated as not to produce respiratory or cardiac embarrassment, paralyse the motor end-plates alone some time after the administration of venom, yet with bigger doses animals die long before paralysis of the end-plates develops. They state that following the injection of large doses of venom in animals, stimulation of the phrenic nerve immediately after death is found to give rise to contraction of the diaphragm, and conclude that lethal doses of Indian cobra venom cause respiratory distress followed by death owing to central respiratory paralysis. The authors make no comment on the most recent experimental work on this subject—notably that of KELLAWAY, who by applying to the phrenic nerve non-polarizable electrodes connected to capacity amplifiers obtained with a loud speaker an audible record of descending motor impulses from the respiratory centre in animals paralysed with colubrid venoms and kept alive by artificial pulmonary ventilation (this *Bulletin*, Vol. 31, p. 99).

Effects of Venoms on the Cardio-Vascular System.—VERNES and KORESSIOS¹⁷ state that in normal people small doses of cobra venom have a hypotensive effect, while in cases of arterial hypertension a fall of blood pressure lasting for some weeks follows the injection of non-toxic amounts of venom. LAIGNEL-LAVASTINE, WÜRMSE and KORESSIOS¹⁸ studied experimentally variations of arterial pressure in the dog, and found a definite hypotensive effect to follow the injection of 1/100–1/50 mgm. of cobra venom per kg. body weight; this hypotensive action persisted after double vagotomy and the injection of atrophine sulphate. After the injection of cobra venom the hypertensive effect of adrenalin was diminished. They concluded that in man the sustained hypotensive action of cobra venom was due to its selective action on the peripheral vessels and was independent of the vagus. GAUTRELET and HALPERN¹⁹ examined frogs injected with cobra venom and showed that during the period of hypotension excitation of the central end of the vago-sympathetic and the sciatic and the application of different substances like adrenalin, choline, nicotine, acetyl-choline and pituitrin indicated that the hypotension was not due to vaso-dilator paralysis. Some evidence in support of the view that there was a direct action on the capillaries comparable to that of histamine was presented. NAKAMURA²⁰ studied

¹⁶ VENKATACHALAM (K.) & RATNAGIRISWARAN (A. N.). Some Experimental Observations on the Venom of the Indian Cobra.—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 289–294. With 1 graph. [14 refs.]

¹⁷ VERNES (Arthur) & KORESSIOS (N. T.). L'action du venin de cobra sur la pression artérielle (homme normal et homme hypertendu).—*Arch. Inst. Prophylactique.* 1934. Vol. 6. No. 1. pp. 20–35. With 14 figs.

¹⁸ LAIGNEL-LAVASTINE, WÜRMSE (Lise) & KORESSIOS (N. T.). Le mécanisme physiologique de l'action hypotensive du venin de cobra.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1934. Apr. 2. 50th Year. 3rd Ser. No. 11. pp. 494–498. With 6 graphs.

¹⁹ GAUTRELET (J.) & HALPERN (N.). Étude expérimentale de l'action du venin de cobra sur la circulation.—*C. R. Soc. Biol.* 1934. Vol. 115. No. 9. pp. 942–943.

²⁰ NAKAMURA (Tutomu). Ueber die Wirkung des Giftes der Naja naja atra auf das isolierte Froschherz. II. Mitteilung: Jahreszeitliche Schwankungen der Resistenz des Froschherzens gegen das Kobragift.—*Taiwan Igakkaï Zasshi (Jl. Med. Assoc. Formosa).* 1934. Feb. Vol. 33. No. 2 (347). [In Japanese pp. 207–211. With 1 chart. German summary p. 17.]

the resistance of the isolated frog's heart to the action of venom of *Naja naja atra* and found the effects varied according to the species of the frog and the season of the year, the toxic effect being accelerated in summer.

GAUTRELET, HALPERN and CORTEGGIANI²¹ find that the intravenous injection of 1/20–1/40 mgm. per kg. of *Vipera aspis* venom in the chloralized dog produces an immediate fall of arterial pressure of 50 to 100 mm. which lasts 1 to 2 hours; the pressure takes 4 to 5 hours to return to its original level. Often there is a diminution in the cardiac output within $\frac{1}{2}$ to 1 hour. This fall in pressure is accompanied by dilatation of the peripheral and intestinal vessels, by contraction of the spleen and kidneys and by an increased viscosity of the blood associated with polycythaemia. The latter phenomenon suggests an increased permeability of the capillaries.

CUBONI²² reports that viperine venom (*Vipera ammodytes*) injected into rabbits intravenously causes an immediate fall in blood pressure, and that specific antiserum when added to the venom inhibits this action; normal horse serum produces the same result, but to a lesser degree. Formalized venom injected intravenously does not affect the blood pressure even when given in large doses.

CHOPRA and CHOWHAN²³ give a detailed account of their work on Indian Daboia venom (*Vipera russellii*) with special reference to its action on the circulatory system. This venom was found to act on the endothelial layers of the blood vessels, particularly the walls of the capillaries, and extensive haemorrhagic phenomena appeared early. There was a marked tendency to produce thrombosis and gangrene at the site of the bite. The systemic blood vessels especially the peripheral ones were contracted, and those of the splanchnic area widely dilated as in histamine shock. The lungs showed haemorrhage, infarction and congestion. The right side of the heart was full of dark blood, there was enormous engorgement of the abdominal viscera and the serous cavities contained much sanguineous fluid. Large doses of venom caused a rapid and permanent fall in blood pressure in both the normal and the decerebrate animal, but when the mesenteric arteries were clamped quite large doses of venom failed to produce any marked hypotensive effect. The fall of blood pressure ordinarily observed could be overcome by pituitrin, adrenalin and large doses of saline. The paralytic action of the venom on the capillaries with increased leakage of fluid into the tissues resembled that of histamine shock, and it was noted that where large doses of histamine were initially injected no further fall of blood pressure followed venom administration. Shock so produced was the main cause of death in Daboia bites.

²¹ GAUTRELET (J.), HALPERN (N.) & CORTEGGIANI (E.). Action du venin de *Vipera aspis* sur la circulation.—*C. R. Soc. Biol.* 1934. Vol. 116. No. 24. pp. 867–868.

²² CUBONI (E.). Il siero antivipera sopprime l'azione ipotensiva del veleno di vipera.—*Boll. Istituto Sieroterap. Milanese*. 1933. Nov. Vol. 12. No. 11. pp. 841–845. With 3 graphs on 2 plates. [18 refs.] German summary.

²³ CHOPRA (R. N.) & CHOWHAN (J. S.). Action of the Indian Daboia (*Vipera russellii*) Venom on the Circulatory System.—*Indian J. Med. Res.* 1934. Jan. Vol. 21. No. 3. pp. 493–506. With 6 figs. [22 refs.]

Effects of Venoms on the Red and White Corpuscles.—VELLARD and MIGUELLOTTE-VIANNA²⁴ studied the venoms of *Lachesis*, *Crotalus* and *Naja* and demonstrated a pronounced lytic effect on red and white corpuscles followed by a stimulating action on the haematopoietic organs characterized by the appearance in the circulation of numbers of immature cells. In poisoning by venom of *Crotalus terrificus* the decrease in the number of red cells was much more evident in the first few hours than with *Lachesis* venom; the numerical increase of leucocytes on the other hand was more marked and persistent. The venom of *Naja tripudians* was more intensely lytic than either of the others. A delayed polymorphonuclear leucocytosis accompanied gangrene or local abscess formation.

HOLDEN²⁵ reports on the effects of variations in the concentration of red cells, variations of the hydrogen ion, the presence of trivalent anion and the addition of certain proteins in modifying haemolysis of rabbits' erythrocytes by copper-head venom. It was found that certain proteins had an inhibiting effect, that haemoglobin accelerated haemolysis, and that the hydrogen ion concentration affected the velocity of lytic action.

The Haemostatic Possibilities of Snake Venom.—Acting on the suggestion of Professor H. HARTRIDGE in regard to coagulants in certain snake venoms, MACFARLANE and BARNETT²⁶ examined the action of various venoms collected from snakes in the London Zoo on haemophilic blood with the view to the production of a haemostatic agent.

Haemophilic blood was obtained from three donors, and to 10 drops of this was added 1 drop of a 1/1,000 solution of the venoms in a mechanical coagulometer, the coagulation time being compared with that of untreated blood. The only genus in which the venoms were consistently coagulant was *Vipera*, and of these *Vipera russellii* yielded the most striking results; thus in 17 seconds it clotted haemophilic blood which took 35 minutes to clot spontaneously. The deleterious effects of other toxic venom constituents were diluted out by employing a 1/10,000 solution, which provided a clotting time of about 60 seconds—sufficient for all practical purposes—and sterility was ensured by passage through a Berkefeld filter No. 12 bV. The authors state that not enough data have accumulated to allow of definite therapeutic claims, but in both dental and general surgery the solution has been applied with apparent success as a haemostatic in both normal and haemophilic subjects without ill-effects. In genuine haemophilic subjects it has been used most effectively following dental extraction (two cases), to control epistaxis (one case), and to control haemorrhage from wounds (one case). The confirmatory clinical reports will be awaited with great interest.

In a further report on the relative potency of certain snake venoms to coagulate haemophilic blood these authors, BARNETT and MACFAR-

²⁴ VELLARD (J.) & MIGUELLOTTE-VIANNA (M.). Action de l'envenimation ophidique sur les globules sanguins.—C. R. Soc. Biol. 1935. Vol. 118. No. 1. pp. 19–20.

²⁵ HOLDEN (Henry Francis). Haemolysis by Australian Snake Venoms. 3. Some Factors which influence the Action of the Venom of the Copperhead.—Australian J. Experim. Biol. & Med. Sci. 1934. June 16. Vol. 12. Pt. 2. pp. 55–61. With 8 figs.

²⁶ MACFARLANE (R. G.) & BARNETT (Burgess). The Haemostatic Possibilities of Snake-Venom.—Lancet. 1934. Nov. 3. pp. 985–987.

LANE,²⁷ point out that the coagulating ferment is present in many more snake venoms than has been supposed. Its presence in Mamba venom and that of the common Krait are instanced as examples, for here its presence could not have been detected had normal instead of haemophilic blood been utilized in experiments.

Other Observations on Venoms.—BERNKOPF²⁸ has studied the effects of formaldehyde on the contraction of the isolated uterus of the guinea-pig caused by snake venom, but unfortunately the species is not given. The previous addition of formaldehyde to the Ringer-Dale solution in which the organ is suspended inhibits the uterine contraction which is normally caused by venom. Renewal of the solution is generally followed by contraction when venom or histamine are added. The author is of the opinion that formaldehyde acts directly on the muscle tissue, and that the delayed contraction of muscle occurs when formaldehyde has been washed out of the bath, leaving the venom or histamine free to act. This is contrary to the view of KENDALL, who ascribes the antagonism between formaldehyde and histamine to chemical reaction.

NECHKOVITCH²⁹ injected cobra venom into the mesenteric and ear veins respectively of dogs, and invariably found that in passing through the liver much of its toxic action was lost. He suggests this is one of the reasons why cobra venom is ineffective when taken *per os*.

PHISALIX and PASTEUR³⁰ investigated the action of shortwave length radiation on the venom of *Vipera aspis*. Its first action was to destroy antigenic properties and to make the venom more toxic: if adequately irradiated, however, the toxicity was reduced by $\frac{1}{3}$ to $\frac{1}{4}$, the haemorrhagin content of the venom remaining unmodified.

VIII. *Clinical Aspects and Treatment.*

LOUNSBERRY³¹ describes a case of rattlesnake anaphylaxis associated with generalized dermatitis. There was a history of having been bitten by a rattlesnake in 1930; the present bite was caused by *Crotalus mitchelli*. Immediately following the bite an itchy, burning, urticarial rash developed: fever, chill and cold sweating followed. Four hours after injection 10 cc. of antivenene were given subcutaneously and two hours later a similar dose intramuscularly. A widespread dermatitis resulted and later developed into a diffuse erythematous papulovesicular eruption with blebs forming at certain points, especially around the site of the bite. In 1930 ZOZAYA and STADELMAN had reported a

²⁷ BARNETT (Burgess) & MACFARLANE (R. G.). On the Relative Potency of Certain Snake-Venoms to coagulate Haemophilic Blood.—Reprinted from *Proc. Zool. Soc.* 1934. Pt. 4. pp. 977-978.

²⁸ BERNKOPF (Hans). Ueber die Wirkung des Formaldehyds auf die durch Schlangengifte hervorruhbare Kontraktion des glatten Muskels.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Sept. 18. Vol. 83. No. 3/4. pp. 197-203.

²⁹ NECHKOVITCH (M.). De l'action anticobraïque du foie—*C. R. Soc. Biol.* 1934. Vol. 115. No. 8. pp. 889-890.

³⁰ PHISALIX (Marie) & PASTEUR (Félix). Action des ondes courtes sur le venin de vipère aspic.—*C. R. Acad. Sci.* 1934. July 16. Vol. 199. No. 3. pp. 235-237.

³¹ LOUNSBERRY (C. Ray). Rattlesnake Anaphylaxis associated with a Generalized Dermatitis.—*Arch. Dermat. & Syph.* 1934. May. Vol. 29. No. 5. pp. 658-667. [18 refs.]

somewhat similar condition in a man who had been inoculated experimentally with venom from *C. mitchelli* and later had been bitten by a copper-head; subsequently he developed a desquamating, eczematous dermatitis whenever he handled dried venom.

FREY³² reports that 13 cases of bites by the common adder (*Vipera berus*) were treated in the Königsberg Hospital in 1933 without any deaths. Such procedures as local incision, sucking the wound and bandaging the limb were deprecated. The only reliable treatment was antivenene (Pasteur Institute E.R.); 10 cc. of this serum were injected intramuscularly into the neighbourhood of the bite, but if dangerous symptoms supervened the dosage was raised to 40 cc. or more and given intravenously; in the latter case it is advised to test the patient for hypersensitiveness to horse serum.

GALLI-VALERIO³³ points out that *Vipera aspis* and *Vipera berus*, but not *Vipera ammodytes*, are encountered in Switzerland. The venom yield is approximately 30 to 40 mgm. in each instance and the actions of the venoms are identical. Opinions differ, however, regarding the frequency of lethal effects on man and different authorities are quoted giving variable death rates. In Switzerland from 1817 to 1886 the mortality rate from bites by these vipers was estimated by FREDER to be 7 per cent., while BRENNING more recently calculated the mortality rate for Europe to be 8.5 per cent. PETITPIERRE³⁴ reviewed 21 cases of venomous snake bite in Switzerland during the past 50 years. The only fatal case was his own: this occurred in a girl aged 10 years who was bitten on the thigh by an adder and brought to hospital about 1½ hours after being bitten. Antivenene could not be obtained from any chemist in the Upper Engadine and though local measures including ligature, cupping and the local injection of 1 per cent. solution of potassium permanganate were employed the child died within 2 days. He advocates ligature above the seat of the bite and the injection of appropriate antivenene as the most suitable treatment. The four antivenenes available in Europe were discussed—Calmette's serum E.R. prepared at the Pasteur Institute from horses immunized with the venoms of *V. berus* and *V. aspis*, Behring serum prepared by immunization with a number of European and non-European venoms, the Vienna anti-bothrops serum prepared with the venom of *Lachesis jararaca*, which KRAUS has shown to neutralize the venoms of the European vipers, and the Milan serum S.M. made by immunization with the venom of *V. ammodytes*. As only *V. berus* and *V. aspis* are found in Switzerland, PETITPIERRE advocates the use of Calmette's serum.

IX. Antivenenes.

PEPEU³⁵ reports his observations on the specificity of three out of these four viperine antivenenes. Mice were used in these experiments

³² FREY (Sigurd). Der Kreuzotterbiss.—*Deut. Med. Woch.* 1934. Feb. 16. Vol. 60. No. 7. pp. 240–242. [13 refs.]

³³ GALLI-VALERIO (B.). Observations sur les morsures de *Vipera aspis*, L.—*Schweiz. Med. Woch.* 1934. Aug. 18. No. 33. pp. 773–774.

³⁴ PETITPIERRE (Marco). Ueber Schlangenbissvergiftungen in der Schweiz mit besonderer Berücksichtigung des Engadins, des Puschlavs und des Bergells.—*Schweiz. Med. Woch.* 1934. Apr. 28. No. 17. pp. 372–380. With 7 figs. (1 plate). [40 refs.]

³⁵ PEPEU (F.). Recherches sur la spécificité des sérums anti-ophidiens.—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1934. Oct. Vol. 6. No. 10. pp. 383–387. [13 refs.]

and the venom and antivenene mixture were kept for 1 hour at 37°C. before intravenous injection. The conclusions reached were that anti-ammodytes and anti-aspid-berus sera neutralized equally all three venoms, that anti-bothrops serum neutralized *V. ammodytes* and *V. lebetina* venoms, but only feebly *V. aspis* venom, and that anti-ammodytes serum can be employed in the treatment of snake poisoning produced by all the European vipers and *V. libetina* of Asia as well. PEFEU³⁶ studied the venom of *V. ammodytes* to which 0.4 per cent. of formalin had been added and after a variable period of incubation at 38°C. found it was transformed into anatoxin. Dogs were actively immunized with anatoxin prepared from half a gland and subsequently inoculated subcutaneously into the paw or snout at intervals of 15 to 34 days with the venom contained in one gland. Complete protection was found provided the venom was injected subcutaneously, but if given intravenously the animal died.

The keeping properties of antivenenes from 1907 to 1925 have been studied by DO AMARAL, ARANTES and DA FONSECA.³⁷ They concluded that the precipitate found in antivenenes is composed of pseudo-globulin and does not seem to exert any appreciable influence on their neutralizing activity. Nor does purification of plasma by fractional precipitation of globulin or the hydrogen ion concentration in the ampoules influence its activity after long keeping. Age *per se* is not an apparent cause of inactivity, which occurs early during the first few years and then appears to remain stationary. Once this initial depreciation of titre has occurred its potency generally remains stationary for 25 years at about 50 per cent. of its original value.

PRATT-JOHNSON³⁸ describes a method of estimating the haemorrhagin content of viperine venom by observing the effects of venom dilutions inoculated intradermally into the depilated skin of albino guineapigs; 0.1 cc. of a series of saline dilutions of dried venom is used, and a fairly sharp end point is reached at which no capillary haemorrhage is produced (negative reaction). The smallest dose of venom which in 30 minutes produces a definite bluish-black area measuring 5 to 10 mm. in diameter is recorded as the minimal skin dose (m.s.d.) for any particular batch of venom.

By mixing falling dilutions of antivenene with a certain skin test dose of viperine venom and after an interval injecting the mixture intradermally the neutralization point is found. Using this technique it is possible to express the potency of the antivenene in terms of its power to neutralize so many minimal skin doses of viperine venom, while the titre of antihaemorrhagin may be observed throughout the course of immunization.

³⁶ PEFEU (F.). Essais de vaccination expérimentale anti-ophidienne.—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia*. Milan. 1934. Oct. Vol. 6. No. 10. pp. 380-382.

³⁷ DO AMARAL (Afranio), ARANTES (J. Bernardino) & DA FONSECA (Flavio). De la durée de l'activité des antitoxines et des antivenins.—*Rev. Sud Américaine de Méd. et de Chirurg.* Paris. 1934. Apr. Vol. 5. No. 4. pp. 209-218. [22 refs.]

³⁸ PRATT-JOHNSON (J.). The Estimation of Haemorrhagin in Venoms by an Intradermal Method and a Potency Test of Antivenomous Serum for Antihaemorrhagin.—*Jl. Path. & Bact.* 1934. Nov. Vol. 39. No. 3. pp. 704-706.

GREVAL³⁹ reviews the production of antivenene in India and describes a technique for concentrating the neutralizing factor in the pseudo-globulin fraction. The pseudo-globulin is separated and dialysed after a fractional precipitation of the blood proteins with ammonium sulphate and the dialysate constitutes the concentrated antivenene. The ammonium sulphate method is said to be cheaper, easier and more efficient than the sodium sulphate method recently advocated for use in India by MAITRA, NAIDU and AHUJA (this *Bulletin*, 1933, Vol. 31, p. 104).
N. Hamilton Fairley.*

*Summaries of the German papers were made by Colonel H. J. WALTON.

³⁹ GREVAL (S. D. S.). Concentration of Antivenene by the Ammonium Sulphate Method.—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 365–371. With 2 figs. on 1 plate.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 6.]

TRYPANOCIDAL AND ANTI-MALARIAL DRUGS.

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(Received March 27, 1935.)

It is a counsel of perfection, which not even the most enthusiastic of organic chemists would urge, to ask medical men to use the systematic, chemical names by which synthetic drugs are described in purely chemical literature. Chemists themselves find these names impossible for daily laboratory use and almost invariably substitute for them such simple designations as a letter, or a name, with a serial number, *e.g.*, B.117 or Galen 45, and new drugs are even submitted for biological tests and clinical trials under these laboratory abbreviations. When the results of such tests are promising the new drug is usually patented and the patentee generally takes the further protective step of registering for it a trade-mark name. When in due course the patent lapses the manufacture of the drug may be taken up by other people, each of whom may register for it a new trade-mark name for the protection of his particular brand of the product. Should the drug be admitted to the Pharmacopoeia or the British Pharmaceutical Codex, the authorities for these publications will coin a new name, which is non-proprietary and available for general use. In these and other ways the present complex synonymy has been built up. The present authors have compiled a list of 21 names, coined by official and unofficial efforts in various countries, for the drug known officially in this country and the United States as nearsphenamine. Glossaries of such names are printed from time to time in pharmaceutical publications, but as a rule these are confined to well-established drugs and perforce cannot include names of drugs which are still in the experimental stage.

It is not practicable to prepare a complete guide to names of drugs which have been tried in malaria and trypanosomiasis, and to which reference may have been made in the literature of these two diseases; in the following paragraphs mention is made only of drugs referred to in reviews, which have appeared in the last 10 years in this *Bulletin*, and which in the authors' experience are frequently the subject of enquiry. It should be understood that many of the names given are trade-marks, and that though the essential component may be the same in different brands of a drug, it does not necessarily follow that all

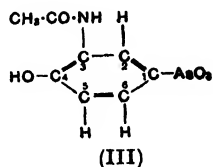
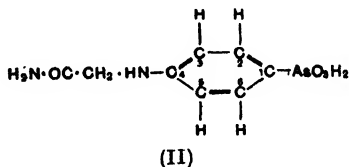
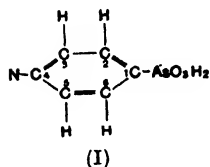
the brands are identical; they may differ in the base associated with an acid or *vice versa*, in the amount of water of crystallization present, in physical condition and in other ways, all of which may influence a physician's choice among them. The systematic chemical names used and the numbering of the positions of substituents in the formulae are based on the rules adopted in the *Journal of the Chemical Society of Great Britain*. The references given are to this *Bulletin* unless stated otherwise.

Quinquevalent (Pentavalent) Arsenic Compounds.—The first arsenical drug used in the treatment of trypanosomiasis was 4-aminophenylarsonic acid (formula I) generally used in the form of the sodium salt and for which the following names are in use:—sodium aminarsonate (B.P.C.), sodium arsanilate, arsamin, atoxyl, soamin, tryproxyl (1932, 29, 642).

An interesting derivative of this substance is 4-phenylglycylamidearsonic acid (formula II), for which the systematic name *N*-phenylglycineamide-*p*-arsonic acid (B.P.C.) is also sometimes used. In the form of its sodium salt this product is known as tryparsamide, other names being tryparsone (B.P.C.), glyphénarsine (1934, 31, 578: Pharm. Belg. iv), tryponarsyl (1928, 25, 790; 1934, 31, 578), tryptan (1933, 30, 786) and novatoxyl (1930, 27, 230).

Other products derived from the same primary substance are 4-hydroxyethylaminophenylarsonic acid (etharsanol) and 4-hydroxypropylaminophenylarsonic acid (proparsanol), also both used as sodium salts (1929, 26, 199). With a hydroxyl group substituted in position 2 and acetylation of the amino group, the primary product becomes 2-hydroxy-4-acetylaminophenylarsonic acid, the sodium salt of which is Fournéau 270 (orsanine; 1932, 29, 640).

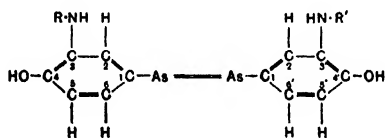
In a second series the position of the amino group in relation to the arsonic acid residue is changed from 4 to 3. The best known member of this group is 4-hydroxy-3-acetylaminophenylarsonic acid (formula III), the diethylamine salt of which is acetylarsan (1927, 24, 569) and the quinine salt quiniostovarsol, whilst the sodium salt is known under the names acetarsol (B.P.C.), acetarsone, kharophen, orarsan, osvarsan (1931, 28, 1010), spirocid and stovarsol. A variant, in which the acetyl group, CH_3CO , is replaced by the formyl radical, is 3-formylamino-4-hydroxyphenylarsonic acid, the sodium salt of which has the names formyphénarsine (Pharm. Belg. iv) and tréparsol (1931, 28, 907).



An isomeride of stovarsol, in which the relative positions of the acetylmino- and hydroxyl groups have been changed, is 2-hydroxy-5-acetylaminophenylarsonic acid, the sodium salt of which is troposan and the quinine salt quinine-troposan (1929, 26, 380).

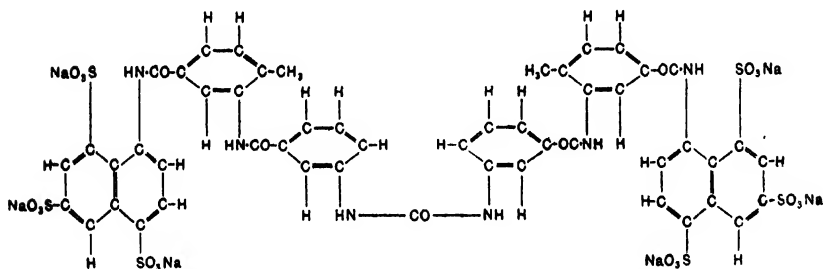
Tervalent (Trivalent) Arsenic Compounds.—The best known of these is 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene dihydrochloride, commonly known as salvarsan or 606, but for which the non-proprietary

name arsphenamine is in common use in the British Empire and the United States. The drug is now generally used in the form of one of its two principal derivatives. The first of these is the *N*-methylene-sulphoxylate (formula IVa), which is neoarsphenamine (B.P.), other names being neoarsenphenolamine, neoarsaminol, neokharsivan, neo-salvarsan (Ehrlich 914), novarsan, novarsenobenzene, novarsenobenzol, novarsenobillon (N.A.B.), novostab, rhodarsan. The second derivative is the *N*:*N'*-dimethylenebisulphite (formula IVb) which is sulpharsphenamine (B.P.) and for which kharsulphan, metarsenobillon, myosalvarsan, sulfarsenol and sulphostab are brand names.



(IVa): R = H; R' = $\cdot\text{CH}_2\cdot\text{O}\cdot\text{SON}$. (IVb): R and R' = $\cdot\text{CH}_2\cdot\text{O}\cdot\text{SO}_2\text{Na}$.

Symmetrical ureas (Carbamides).—The first and best known of this group of trypanocidal drugs is Bayer 205 or germanin. Its constitution was not disclosed by the proprietors, and in 1924 FOURNEAU and collaborators (1924, 21, 379) described the production of a symmetrical urea of *m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-1-naphthylamino-4:6:8-trisulphonate of sodium (formula V), which is now manufactured in France under the name Fourneau 309 (moranyl). As to the relationship of this substance to germanin, BAUER and BECKER have stated (1930, 27, 67) that there can hardly be any doubt that Fourneau has found the right formula. According to a preliminary announcement (*Chemistry and Industry*, 1934, 53, 836) the systematic name given above also applies to antrypol. Naganol is a form of germanin for veterinary use.



(V)

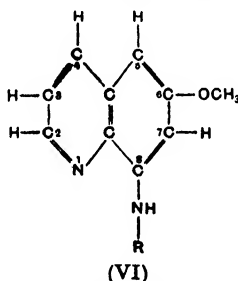
Alkaloids.—Though a number of drugs used by natives in the Tropics as anti-malarials have been examined in recent years and found to yield characteristic and well-defined alkaloids, none of these has proved of sufficient activity to come into use, and the cinchona alkaloids remain the sole anti-malarials of this group. Even these familiar substances have added to the nomenclature of drugs, as the result of efforts to present them in more advantageous forms.

Tebetren is said to be "compounded of derivatives of quinine, acridine, etc., for the treatment and prophylaxis of malaria," whilst another

statement describes it as "prepared by a special process, combining acridine and quinine derivatives with a derivative of cholic acid" (cf. 1933, 30, 84; 1934, 31, 693). Malarcan seems to be a similar product (1935, 32, 113).

The mixture of crystalline cinchona alkaloids known as quinetum has been given a definite modern standard by the Malaria Commission of the League of Nations, who have also rendered cinchona febrifuge unnecessary by the introduction of the improved and standardized mixture known as totaquina (1932, 29, 461). Variants and precursors of totaquina in which the bases are converted into sulphates producing a more soluble product are panchina (1929, 26, 23) and the chineto No. 1 issued by the Italian State Factory (1932, 29, 712). Where cinchona febrifuge is still used, it is perhaps worth while to remind medical men of the useful standard suggested for this drug by FLETCHER (Notes on the Treatment of Malaria with Alkaloids of Cinchona, London, 1923, p. 3), though it is to be hoped that the recommendation of the Malaria Commission of the League of Nations (*loc. cit.*) that cinchona febrifuge should be replaced by totaquina will be generally acted upon.

Quinoline Derivatives.—The introduction of beprochin, since re-named plasmoquine, gave an enormous stimulus to the search for new anti-malarials. Although the starting point of the investigation which eventually led to plasmoquine is stated to have been methylene blue, plasmoquine has a closer relationship to quinine than to methylene blue. Its constitution was announced officially in 1928 (*Arch. f. Schiffs- u. Trop.-Hyg.*, 1928, 32, 382) as 6-methoxy-8-diethylamino-isopentylaminoquinoline, and a considerable number of similarly-constituted drugs have been synthesized in recent years in this country, France and Russia. Those that have been tried clinically are for the most part 6-methoxyquinolines with a dialkylaminoalkylamino- side chain in position 8 (see formula VI) and, as the following table shows, it is the length and nature of this chain which is the principal source of variation.



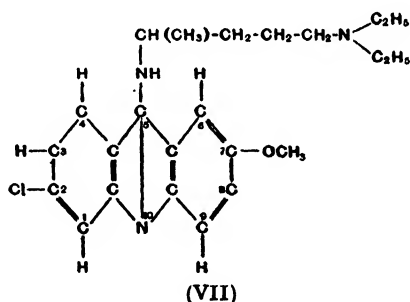
In plasmoquine $R = -CH(CH_3).CH_2.CH_2.CH_2.N(C_2H_5)_2$.
In related substances its character is as shown in the table below.

Name of Drug.			Character of side-chain.
Plasmoquine	$.NH.CH(CH_3).CH_2.CH_2.CH_2.N(C_2H_5)_2$.
Fourneau 710 (Rhodoquine)	$.NH.CH_2.CH_2.CH_2.N(C_2H_5)_2$. (1932, 29, 348).
Fourneau 574	$.NH.CH_2.CH_2.CH_2.N(CH_3)_3$. (1933, 30, 849, 850).
Fourneau 664	$.NH.CH_2.C(CH_3)_2.CH_2.N(C_2H_5)_2$. (<i>Ann. Inst. Pasteur</i> , 1931, 46, 537).
Fourneau 852	$.NH.(CH_2)_{11}.N(C_2H_5)_2$. (1934, 31, 175).

The Russian product plasmocide is described by the same chemical name as Fournau 710 (1934, 31, 174, 698). Fournau 852 is also issued with sodium stovarsol as Fournau 915 or Rhodoquine U (1933, 30, 850 : 1934, 31, 432, 433).

Acridine Derivatives.—A considerable number of reviews in this *Bulletin* deal with peracrina 303 as an anti-malarial drug. This product is stated to be a preparation of 2:8-diamino-10-methyl-acridinium chloride, which is acriflavine (B.P.), also known as tryptaflavine and gonacrine. Acridine derivatives are also stated to be present in tebetren and malarcan in admixture with a cinchona alkaloid (*see above*).

The success which attended the insertion of a dialkylamino-alkylamino- side-chain in 6-methoxyquinoline, naturally led to the examination of the results of such insertions in other heterocyclic nuclei, and from this arose atebirin, which is 2-chloro-5-diethylamino-isopentylamino-7-methoxyacridine (MAUSS and MIETZSCH, *Klin. Woch.*, 1933, 12, 1276). Atebrin, therefore, contains the same side-chain as plasmquine with the 6-methoxyquinoline nucleus of the latter replaced by a 2-chloro-7-methoxyacridine nucleus (formula VII). The constitutional name assigned to quinacrine (1934, 31, 698) is identical with that of atebirin.



Names of Substances mentioned.

Name of Substance.	Page	Name of Substance.	Page
Acetarsol	386	Fournau 664	388
Acetarsone	386	„ 710	388
Acetylarsan	386	„ 852	388
Acriflavine	389	„ 915	389
Antrypol	387	Germanin	387
Arsamin	386	Glyphénarsine	386
Arsphenamine	387	Gonacrine	389
Atebrin	389	Kharophen	386
Atoxyl	386	Kharsulphan	387
Bayer 205	387	Malarcan	388
Beprochin	388	Metarsenobillon	387
Chineto No. 1	388	Moranyl	387
Ehrlich 914	387	Myosalvarsan	387
Etharsanol	386	Naganol	387
Formyphénarsine	386	Neoarsaminol	387
Fournau 270	386	Neoarsenphenolamine	387
„ 309	387	Neoarsphenamine	387
„ 574	388	Neokharsivan	387

Name of Substance.	Page	Name of Substance.	Page
Neosalvarsan	387	Rhodoquine U	389
Novarsan	387		
Novarsenobenzene	387	Salvarsan	386
Novarsenobenzol	387	Soamin	386
Novarsenobillon	387	Sodium aminarsonate	386
Novatoxyl	386	Sodium arsanilate	386
Novostab	387	Spirocid	386
Orarsan	386	Stovarsol	386
Orsanine	386	Sulfarsenol	387
Osvarsan	386	Sulpharsphenamine	387
Panchina	388	Sulphostab	387
Peracrina 303	389		
Plasmocide	389	Tebetren	387
Plasmoquine... ..	388	Totaquina	388
Proparsanol	386	Tréparsol	386
Quinacrine	389	Troposan	386
Quinetum	388	Trypaflavine	389
Quinine-troposan	386	Tryparsamide	386
Quiniostovarsol	386	Tryparsone	386
Rhodarsan	387	Tryponarsyl	386
Rhodoquine	388	Trypotan	386
		Trypoxyl	386

MALARIA.

GREEN (Richard). **Lectures on the Development and Use of the Synthetic Anti-Malarial Drugs.**—*Bull. Inst. Med. Res. Federated Malay States*. 1934. No. 2. pp. iv+50. With 7 figs. [39 refs.]

A useful paper on the history and efficiency of these drugs. Fewer recrudescences occur after atebirin than after quinine.

About 80 years ago, a search was begun for a synthetic substitute for quinine, and, in 1856, while PERKIN was engaged in this work he accidentally discovered the first of the coal-tar dyes. Eleven or twelve years ago, research on the problem of evolving a synthetic drug for malaria was, in general, mainly a matter of : (1) Trying to build up the molecule of quinine by synthetic means. (2) Modifying the structure of EHRLICH's anti-syphilitic arsenicals, so that they would destroy not only the benign tertian parasite, but the subtertian and quartan parasites as well. (3) Modifying the structure of methylene blue so that its action on the quartan parasite would be stronger, and so that it would also be effective against the benign tertian and subtertian parasites. Attempts to build up the molecule of quinine continued to fail. Stovarsol was evolved as a "spirocidal" drug, but was found also to be effective in benign tertian malaria when given by the mouth; it had to be combined with quinine for treating subtertian and quartan malaria. Thousands of different compounds were evolved. Fortunately the malaria of birds gave some indication of the antimalarial efficacy of these drugs, and the technique evolved by ROEHL at Elberfeld paved the way for the discovery of plasmoquine and atebirin.

Starting with the observation that methylene blue has some anti-malarial action, SCHULEMANN and his colleagues replaced one of the short dimethylamino- side chains, $-N(CH_3)_2$, of this dye-stuff by the longer chain $-N(CH_3).CH_2.CH_2.N(C_2H_5)_2$, thus enhancing the anti-malarial action. It was an obvious step to repeat the experiment with the quinoline, instead of the methylene blue, nucleus and after that to try the effect of changes in the position, length and character of this substituent, the part of the research which led to plasmoquine (see figure VI, HENRY and GRAY's article, p. 388), and, this point being settled, to try the selected substituent in other heterocyclic nuclei including acridine, which led eventually to atebirin (see figure VII, p. 389).

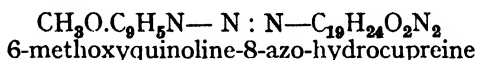
It soon became established that plasmoquine had little or no action on the rings and schizonts of subtertian, and next a reversion was made to a triple ring system instead of the double ring system of the quinoline nucleus. The triple ring system, however, which was finally used was that of acridine instead of methylene blue, and atebirin was the result. It is said that the widening of the ring system in atebirin was aimed at with the object of getting rid of the toxic properties associated with the quinoline nucleus.

The ring system is similar in quinine and plasmoquine—each drug has a quinoline nucleus—although it will be noted that the ring system (or quinoline nucleus) of plasmoquine has undergone, as it were, a complete turn through half a circle prior to being linked up. In atebirin the ring system is different, atebirin has an acridine nucleus. The basic side-chains of plasmoquine and atebirin are identical, that of quinine is distinct and highly complex.

FOURNEAU and his colleagues have produced a large series of compounds of which about 40 have some effect upon the malaria of birds. Certain of these compounds were selected for tests on man; for example Fourneau 710, 574, 852 and 915 (see HENRY and GRAY's article, pp. 330, 388, 389). Both 710 and 574 act like plasmoquine; they have all its defects and are somewhat less effective as regards their action on the benign tertian and quartan parasites. Fourneau 852 is said to be less toxic and to be active against all forms of malarial parasites. Fourneau 710 is easier to prepare than plasmoquine.

Russian chemists have produced a compound which they call "Plasmocide" or "Antimalarene B." It acts like plasmoquine. English workers have recently evolved a number of new quinoline compounds. As judged from tests on birds the results with two of them are regarded as encouraging, but they seem likely to produce methaemoglobinaemia, as plasmoquine does.

The quinine derivative (C.77) prepared experimentally by Professor GIEMSA is a red azo-dye, made by coupling hydrocupreine (hydroquinine is the methyl ether of hydrocupreine, just as quinine is the methyl ether of cupreine) with diazotised 6-methoxy-8-amino-quinoline and may be represented by the simple linear formula :—



The author has treated 21 cases with it. It appeared to act like quinine on the parasites of subtertian and quartan malaria, but to be definitely inferior in benign tertian. It was free from such side effects as deafness, tinnitus, etc. The dose given was about 9 grains daily for 7 days.

Totaquina, tebetren and esanofele, are dealt with under the section of "Drugs containing quinine." "Clinically totaquina is slightly less efficacious than quinine but could replace it in many circumstances." Tebetren is said to consist of a mixture of hydroquinine, acriflavine and bile salts. The author writes "Tebetren is . . . five times more costly than quinine and is no better than quinine in its effect on relapses.

. . . I have been unable to find any reasons on the grounds of increased efficiency or lessened toxicity for substituting such an expensive drug for quinine or atebtrin." Esanofele is widely advertised as a specific for malaria. The composition of each pill is said to be as follows: Quinine bisulphate gr. 1/3, Arsenious acid gr. 1/100, Citrate of iron gr. 2/5. The danger lies in esanofele being accepted as a remedy for acute attacks, while it is really a pill for use in convalescence.

As regards the use of plasmoquine as a means of reducing the transmission of malaria, the author writes :—"It will be noted that the only known successes have been achieved when the *whole* population has been under *regular and continuous* plasmoquine treatment, also that any good results have been lost within a short time after such regular treatment of the whole population has ceased . . . it would seem that anti-gametocyte measures should remain subordinate to anti-larval measures until it can be shown that, in the particular circumstances, better results can be achieved more conveniently, with similar certainty, and at less cost by the use of synthetic drugs. How to *combine* the two measures successfully would appear to be a matter entirely for local judgment in each case."

"Atebrin," he writes, "is the first available drug which can be used in giving effective 'mass' treatments to a large working population, because

it can be given in 'curative' doses at one daily muster and does not interfere with working efficiency as quinine does when given in 'curative' doses. . . . A small but certain proportion of patients under treatment with atebtrin have shown: (a) *Unpleasant by-effects* consisting of (1) mild headache; (2) Mild abdominal pains; (3) Yellowish discoloration of the skin or whites of the eyes. Such symptoms or signs have occurred in about 2 per cent. of patients under my care. Some of these patients, however, were given larger doses, or longer courses, of the drug than usual. . . . (b) *Toxic symptoms*. Under this heading are included: (1) Severe and persistent headache; (2) Severe abdominal pains; (3) So-called 'cerebral excitation.' Such symptoms have occurred in about 1 per cent. of my patients some of whom, again, were given larger doses or longer courses of the drug than usual. . . . The term 'cerebral excitation' requires some further explanation. Briefly, it consists of an excited mental state lasting sometimes about 24 hours or longer. Such a condition occurred in two of my patients, both of whom were treated for severe sub-tertian malaria with atebtrin for a period of 7 days. One case will be described. . . . Treatment with atebtrin, 3 tablets daily, was continued for 7 days. . . . he entered upon a curious phase. . . . 6 days after the course had ended. . . . sang and danced in the ward, appeared to find the greatest amusement in everything going on round him, laughed frequently without apparent cause, and appeared to be in a generally hilarious state. He remained like this for about 24 hours and 'settled down' during the following day. . . . said he felt as if he had been drunk."

Dr. Green considers that before forming any opinion on the use of *Atebtrin as a Clinical Prophylactic*, it would be necessary to have the results of prolonged and well conducted experiments. He does not think that it would be safe to give sub-curative doses of atebtrin, say 0.1 gram daily, over long periods, because of possible cumulative effects. In connexion with the *Prevention of Relapses by Atebtrin*, he treated 63 cases with 3 tablets of atebtrin daily for seven days and observed them for a subsequent period of 27 days; 3 cases or 4 per cent. relapsed. A control series of 53 cases was treated with 30 grains of quinine daily for 7 days. They were then observed for an average period of 18 days only, and 20 cases or 38 per cent. relapsed. The vast majority of patients in the tropics are available for treatment for short periods only (usually not more than 7 days). W. Fletcher.

UNION OF SOUTH AFRICA. ANNUAL REPORT OF THE DEPARTMENT OF PUBLIC HEALTH YEAR ENDED 30TH JUNE, 1934. [*Malaria* pp. 45-58.]

The principal anti-malaria measure adopted is the killing of adult mosquitoes in dwellings by means of a spray.

The 1933-4 season was exceptionally wet, warm weather persisted a month over time into May, breeding of *A. gambiae* occurred on a large scale, cases of fever appeared over a wide area and there were some cases of blackwater fever. The proportion of deaths was much lower than in the past, and this is attributed to the fact that the whole population is gaining knowledge of malaria control and is turning its attention to preventive measures on an organized basis in addition to fighting the disease by immediate treatment as soon as it occurs. Killing adult mosquitoes in dwellings by spraying is the chief method of control. Mosquitoes are easily destroyed in the typical Zulu beehive hut which is usually smoke-laden. The insecticide used is "Pyagra," which is diluted 1 in 17 with paraffin and applied by means of a spray pump. General larval control is impracticable in most native reserves,

but there is hope of solving the malaria problem by supervised spraying, with or without limited larval control. Malaria is endemic in some of the reserves, and the natives have acquired a certain degree of immunity which makes them of special value for work on sugar estates where conditions are unsuitable for non-immune labour. Following the advice of Professor SWELLENGREBEL, no anti-malaria work is being attempted in those reserves with an immune population. Elsewhere, a great deal of propaganda has been carried on; at first the people were suspicious, or even hostile, until the effects of treatment were noted. "It has been shown that anti-malaria control is perfectly feasible in a native area, always provided that it has had a sharp epidemic as a preliminary and that methods of control are introduced tactfully." The mass of the population takes tablet quinine. There has been opposition instigated by native herbalists, but now most of them sell quinine themselves under some disguise or other. One of them pointed out to his customers that whereas the Government supplies were undoubtedly suited to white people, because they had white skins, his medicine had a black spot without which the tablets were useless for natives. He had bored a hole in each tablet and filled it with a mixture of soot and fat.

W. F.

ANNECKE (S.). **Malaria Control in the Transvaal.**—*South African Med. Jl.* 1935. Jan. 12. Vol. 9. No. 1. pp. 3-7.

This deals with gambiae-malaria and funestus-malaria. The people need food rather than advice.

Control of malaria along modern lines has been established only recently in this province, more especially since the receipt of a report to the government by Dr. SWELLENGREBEL. There are two main vectors, (1) *A. gambiae*, the puddle-breeder, breeds in shallow depressions in the ground which are clear of vegetation and exposed to sunlight. It spreads with rainfall. The malaria of the Bushveld is gambiae-malaria. (2) *A. funestus* breeds at the edges of streams or rivers, where shade is plentiful and the current is slow. The malaria of the Lowveldt is funestus-malaria. In gambiae areas antilarval work is put first, because the puddles can be dealt with by draining, filling, or oiling with waste engine-oil to which a little paraffin has been added. In funestus areas, antilarval work is hopelessly impossible from a financial point of view. In these places anti-adult measures such as screening and insecticides must be adopted. "The difficult times through which farmers have passed have left in their wake a mass of people who, though not actually starving, are in very straitened financial circumstances. . . . We teach prevention, and in many homes there is not the wherewithal to buy the daily mealie meal, let alone think about prevention of malaria. Proper feeding . . . is most important in fighting the continual ravages of recurring malaria." The author has a staff of health visitors who visit the homes and give instruction in diet, domestic hygiene and child-welfare. He has drawn up a standard antimalarial treatment which is being adopted by district surgeons, and by practitioners in malarious areas. The control unit of the Department of Public Health does not act executively; it spends no money in the control of malaria, but visits the farms, gives advice and makes inquiries.

W. F.

ANNING (C. C. P.). **Meteorological Factors in the Incidence of Malaria in Pietermaritzburg.**—*South African Med. Jl.* 1934. Dec. 8. Vol. 8. No. 23. pp. 875–878. With 3 charts.

Malaria has spread to Pietermaritzburg which was free from it until about 6 years ago.

The author discusses the possible causes of the spread of malaria from the coast to Pietermaritzburg. The town lies about 50 miles inland at an elevation of 2,100 ft. above sea-level, in a valley surrounded by hills. Several cases of malaria are said to have occurred in 1906, but the evidence is unreliable. No further case infected within the borough was reported until 1929, when a few cases occurred in the eastern side of the town nearest to the coast. There is no record of the number of infections in 1930 and 1931, because notification was not in force, but, between January and May 1932, at least 1,500 new infections occurred. The deaths due to malaria among borough residents were :— 1929, nil; 1930, 3; 1931, 20; 1932, 105; 1933, 25. Extensive drainage and anti-larval and anti-mosquito measures were undertaken in 1933; “to these, to a large extent, is ascribed the marked reduction in the number of infections during the 1933 season.” The vector is *A. costalis*, and the principal breeding places have been in muddy water exposed to the sun. It is difficult to understand why malaria has spread to the healthy town from the coast where it is endemic. The author writes :—

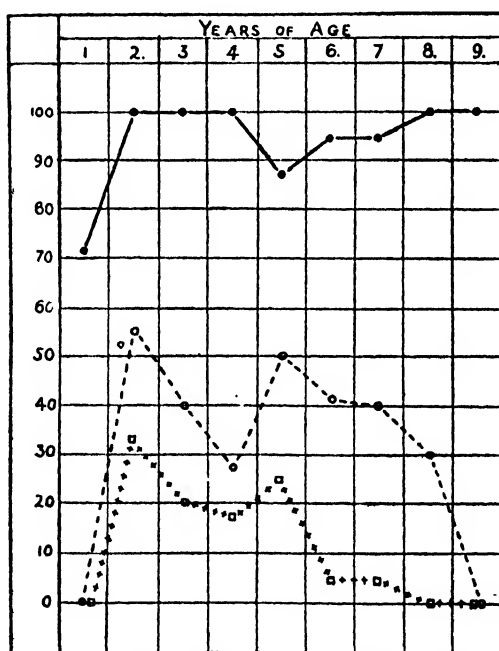
“How far the gradual reduction in total rainfall, associated with an increase during March (the centre of the breeding season), together with a fall in the mean daily temperature during the breeding months of January–April, and a fall in the relative humidity figures for the same period, has made more easy the settlement of *A. costalis* in Pietermaritzburg, I cannot assess . . . The incrimination of road and rail transport as regards the importation of *A. costalis* into Maritzburg rests upon unproven accusations.”
W. F.

THOMSON (J. Gordon). **Malaria in Nyasaland.**—*Proc. Roy. Soc. Med.* 1935. Feb. Vol. 28. No. 4. pp. 391–403 (Sect. Trop. Dis. & Parasit. pp. 11–23). With 4 charts. [35 refs.]

A. gambiae is a more important vector than *A. funestus*. Inherited immunity and tolerance exist among natives. Little illness is caused by infection in older children and adults, but many infants die. Prophylactic quinine should be taken by Europeans.

The chief vectors of malaria in Nyasaland are *A. gambiae* and *A. funestus*. The months of June, July and August are practically rainless; *A. gambiae* disappears and though *A. funestus* is plentiful there is very little malaria. The rains begin in October, swarms of *A. gambiae* appear, malaria increases rapidly and, later on, cases of blackwater fever occur. There have been 157 cases of blackwater in 23 years, with a case mortality of 30 per cent. The cases occur outside the areas controlled by European communities, principally among people who neglect to take precautions and “neither protect themselves from the onslaught of mosquitoes, nor take quinine as it should be taken.” An examination of 103 children made once a month for a whole year showed that some were much more susceptible than others. Four of the children remained consistently negative. This varied resistance in children under 10 years seems to indicate that certain individuals have an inherited tolerance; it has been estimated that only 10 per

cent. live to the age of 6 years*, and possibly it is to a large extent those with inherited tolerance who reach adult age. *P. falciparum* was present in 96 of the 99 infected children, *P. malariae* in 35, and *P. vivax* in 9. During the height of the malaria season, native children up to the age of 2 years frequently have as many as 3 or 4 parasites to one red cell, and many of them die from convulsions. Tolerance is soon developed, and, except in very young children, malaria causes little illness. The children seen in this survey showed few manifestations of malaria and all those who were old enough to walk could run about as if they were perfectly healthy, although they had parasites in their blood. No cases of congenital infection were seen, and the author concludes that "malaria contracted *in utero* is a rarity. . . . The phagocytic picture exhibited by . . . placental smears affords a remarkable demonstration of the active part played by the large mononuclear macrophages and the polymorphonuclear leucocytes as controlling factors, modifying the course of the infection." *P. vivax* infections decrease as age increases, and show the most rapid fall; this is followed by a drop in quartan, but *P. falciparum* persists till at least 9 years of age, without showing any fall in the numbers infected, see Chart. Gametocytes are most numerous in children who are 2 or 3 years old,



●—● MALIGNANT TERTIAN. □---□ BENIGN TERTIAN.

○---○ QUARTAN.

Percentage of children infected, according to age. (Based on monthly examinations of a group of 103 native children in Nyasaland throughout the year.)

[Reproduced from the *Proceedings of the Royal Society of Medicine.*]

* This ninefold decimation of young children is almost Herodian. The Annual Report (1932) gives the estimated death-rate as about 400 per 1,000 live births, up to the age of 6 years, which is surely high enough. [See this *Bulletin*, 1933, Supp., p. 57*.]

and they decrease as the children become older. The gradual development of resistance to infection is also shown by the fall in the spleen rate between the ages of 5 and 10 years.

A dose of 5 grains of quinine should be taken with absolute regularity by Europeans as a prophylactic wherever malaria is hyperendemic, the population scattered, and protection from malaria difficult. Monseigneur Guilleinié published his experiences of blackwater fever in the "Nyasaland Times" in 1934. The White Fathers began to establish Central African Missions in 1878, and during the succeeding 28 years, 200 of them died from blackwater. During the last 28 years they have taken prophylactic quinine, and none of them has died from blackwater.

W. F.

FOLEY (H.) & PARROT (L.). L'assainissement de l'oasis d'El Goléa. La question du paludisme. [**The Sanitation of the Oasis of El Golea.**—*Arch. Inst. Pasteur d'Algérie*. 1934. Dec. Vol. 12. No. 4. pp. 471–484. With 6 figs. on 3 plates & 1 plan.

The sinking of numerous artesian wells has led to the formation of lakes and swamps, which give rise to malaria.

The oasis of El Golea is one of the most beautiful in the Algerian Sahara. It was healthy when it was first occupied by the French in 1891, but malaria followed the introduction of irrigation, and in the year following the sinking of artesian wells there were 68 cases; in 1907 there were 500 cases; in 1927 there was an epidemic of subtertian. A survey made by the authors showed that the disease was not very intense at the present time, but that there were numerous marshes and lakes in which the larvae of *A. multicolor* and *A. sergenti* were breeding. They consider that oiling, the introduction of larvivorous fish and the like, would be of little use. What is needed is the supervision and regulation of irrigation, and the provision of efficient drainage to carry off the water.

W. F.

EGYPTIAN GOVERNMENT. **Anti-Malaria Commission. Report No. 9 of the Anti-Malaria Commission for the Fiscal Year 1932–1933.**—8 pp. With 4 folding plans. 1934. Cairo: Govt. Press, Bulâq. [P.T.5.]

Gives the number of cases of malaria reported in Cairo and other towns.

The Ministry of Finance granted L.E.10,000 for anti-malaria work during 1932–33. The amount spent was L.E.8,116, and this report shows how the sum was distributed among the different towns and villages. In a village near Cairo where three swamps were filled, the contractor obtained the necessary earth from borrow-pits. "The Main-drainage Department placed the amount due to him in suspense account pending the filling in of these borrow-pits." Nearly 200,000 larvivorous fish (*Bolti*, *Cyprinodon*, *Gambusia*) were distributed in swamps and water channels. The number of cases of malaria reported to the Public Health Administration, during the year 1932, was 1,343 with 23 deaths. Sixty-two cases with no deaths, were reported from Cairo; 232 cases, 2 deaths, from Alexandria; 36 cases, 7 deaths from Ismailia; 15 cases, no deaths, from Port Said; 89 cases, 2 deaths, from Suez.

W. F.

KHALIL Bey (M.). **Combatting Mosquitoes and Malaria in Alexandria and its Environments.** (A Report to H.E. the Undersecretary of State for Public Health.)—*Jl. Egyptian Med. Assoc.* 1934. Dec. Vol. 17. No. 12. pp. 943-958.

The incidence of malaria in Alexandria during the last four years was as follows :—1931, 98 cases ; 1932, 282 ; 1933, 303 ; first half of 1934, 143. " Antimalaria projects are not welcomed by administrators . . . administrators prefer the erection of edifices such as a club, a hospital, a museum or a road like the Corniche or a public garden, because such projects are always before the public eye. . . . Malaria can be controlled with success in Alexandria if the necessary means are available."

W. F.

KNOWLES (R.) & BASU (B. C.). **Mosquito Prevalence and Mosquito-borne Diseases in Calcutta City.**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 291-319. With 11 charts & 1 fig. [38 refs.]

Malaria in Calcutta is attributed to the poor water supply.

The authors give in this paper the results of observations carried out in an area, one square mile in extent, around the School of Tropical Medicine in the centre of Calcutta. " Malaria is not apparently a very serious danger to Calcutta City, but we have already one virulent mosquito carrier—*Anopheles stephensi*—breeding in almost every other water storage receptacle in the city, together with the recent introduction of a second, and even more virulent carrier, *Anopheles sundaicus* (*A. ludlowi*). The future is quite uncertain." *A. stephensi* breeds, for the most part, in vessels which are used for storing water ; *Aedes aegypti*, the carrier of dengue, and *Culex fatigans*, the carrier of filariasis, breed in the same places as *A. stephensi*. The low pressure and intermittent character of the water supply are responsible for the prevalence of mosquito-borne diseases in Calcutta. The remedy is the provision of a continuous water supply at high pressure. A figure given in the text shows 21 different kinds of receptacles in which *A. stephensi* was found.

W. F.

BASU (B. C.). **A Brief Survey of Malaria and Anopheline Fauna in Patna.**—Reprinted from *Patna Jl. of Med.* 1933. July. Vol. 8. No. 3. pp. 152-160. With 5 figs.

An increase of malaria due to interference with drainage.

Patna is the capital of Bihar and Orissa. It extends for 15 miles along a narrow strip of land, about a mile wide, compressed between the Ganges on the north and the East Indian Railway line on the south. The malaria curve almost coincides with that of the rainfall ; it rises in the spring, reaches its maximum in August, and then falls. The principal carriers of malaria are (1) *A. culicifacies*, which breeds in the railway ditches and in the borrow-pits of brickfields, and (2) *A. fuliginosus* which breeds in the lakes, ponds and ditches. The prevailing type of malaria is subtertian. *A. stephensi* was not found, although there are innumerable wells and water receptacles because only a part of the town is provided with a water supply and even that is intermittent. The town slopes away from the river, and the drainage runs into a swamp on the south of the railway ; when the Ganges is in flood,

a large part of the town lies below its level. In former days, the swamp drained into the river ; the author implies that, since this drainage has been blocked, there has been an increase of malaria and a decrease in the population. W. F.

COVELL (G.) & BAILY (J. D.). **Malaria in Sind. Part XII. A Note on Malaria in a Water-Logged Area in Khairpur State.**—*Records of the Malaria Survey of India*. 1934. Sept. Vol. 4. No. 3. pp. 327-341.

Increase of malaria attributed to waterlogging due to irrigation by the Lloyd Barrage.

The south-eastern portion of the State is part of a great desert supporting a scrubby vegetation which affords grazing to camels. The north-western part is very fertile where it is irrigated. The average rainfall for the last 13 years is less than 4 inches. The climate is cold in winter, when severe frosts are not unknown, but in summer it is very hot and the thermometer may rise to 120°F. As the result of seepage from the great new Rohri Canal, a considerable area in Khairpur State became completely waterlogged almost immediately after the opening of the Lloyd Barrage in 1932. A survey made in December 1933 showed that the spleen-rate in 14 water-logged villages was 86 per cent. In 11 which were not water-logged it was 63 per cent. A remarkable feature of the survey was the great preponderance of *A. stephensi* over the other species of anophelines captured. The authors consider that the great rise in the subsoil water, following the Barrage, has been the direct cause of the increase of malaria. W. F.

NURSING (D.), RAO (B. A.) & SWEET (W. C.). **Notes on Malaria in Mysore State. Part VII. The Anopheline Transmitters of Malaria.**—*Records of the Malaria Survey of India*. 1934. Sept. Vol. 4. No. 3. pp. 243-251.

Anopheles were caught in an endemic area in houses and cattle sheds, and in a tent with a human bait. They were caught in one district during an epidemic. The authors conclude that *A. culicifacies* and *A. fluviatilis* are the important carriers in the rural areas of Mysore. The former appears to use habitations as a daytime resting place, the latter prefers other situations. In the endemic area, the oöcyst rate of *A. culicifacies* was 2·5 and the sporozoite rate 0·2 per cent., the corresponding rates for *A. fluviatilis* were 2·4 and 0·8 per cent. In the epidemic area, infections were found in *A. culicifacies* only ; the rates being 2·3 per cent. for oöcysts, and 1·0 per cent. for sporozoites. W. F.

CLEMESHA (W. W.). **Brief Account of the Natural History of Malaria in Ceylon.**—*Ceylon Jl. Sci.* (Sect. D. Med. Sci.). 1934. Dec. 8. Vol. 3. Pt. 3. pp. 157-172. With 2 graphs (1 folding).

Malaria in Ceylon occurs at the end of the dry season. When there is plenty of rain there is little malaria.

There is only one carrier in Ceylon, *A. culicifacies*. Other anopheles occur which are important vectors in other countries, for example *A. maculatus* and *A. funestus*, but here they do not bite man. *A. culicifacies* breeds in shallow pools and puddles in the beds of streams when

they are almost empty during dry weather, particularly in flat country at the foot of the hills. It is useless to look for the larvae except in sunny places, and the water must be clear. The normal increase of this species takes place in the hot weather immediately preceding the rains. In the northern part of the island, the dry weather and the period of increase of *A. culicifacies* occur in July, August and September. In the south-east, the period of drought and anopheline breeding is February, March and April. In the south-west part of the island droughts are very rare, and so is malaria. [It is in this district that the great epidemic has occurred following a drought.] *A. culicifacies* is a domestic mosquito; when its normal breeding places are not available it will seek others. Where there are no streams, or where these are polluted, it will breed in wells. It does not breed in paddy-fields, and these are not a cause of malaria in Ceylon. The healthy years in Ceylon are always those in which the July, August and September rainfall is plentiful, that is to say above 20 inches. Unhealthy years are those in which it is scarce, or under 20 inches. W. F.

DANG-HANH-KIÊN. Le paludisme à Phong-Thô. [**Malaria at Phong-Tho.**—*Bull. Acad. Méd.* 1935. Feb. 5. 99th Year. 3rd Ser. Vol. 113. No. 5. pp. 183-191.]

This describes the premunition of the indigenous tribes.

Phong-Tho is one of the most unhealthy districts of Upper Tonking, and can be reached only after a long and dangerous journey through virgin jungle and along precipitous mountain sides. Though the total population numbers only about 12,000, it comprises several races which differ in their languages and customs. Everyone becomes infected with malaria, but the indigenous natives suffer comparatively little inconvenience from it, and the adult splenic index is only 19 per cent. The immigrant Europeans and Annamites, on the contrary, suffer severely; blackwater fever is not uncommon among them and occurs independently of quinine. The adult splenic index is nearly 4 times higher than that of the indigenous races. The author carries out his work in the face of great difficulties. He sees his patients in a shed which leaks in the rainy weather; if he decides to treat any of them as in-patients he must provide for their maintenance at his own cost; he has no microscope; he suffers from malaria. One feels on reading this paper that it is a message from a brave colleague. W. F.

ROBIN (L. A.). Évolution de l'état sanitaire des collectivités ouvrières agricoles importées en région d'hyperendémie palustre. Influence de la "prémunition acquise." [**The Influence of Premunition on the Development of Healthy Conditions among Labourers in Hyperendemic Areas.**—*Rev. d'Hyg. et de Méd. Preventive.* 1935. Jan. Vol. 57. No. 1. pp. 30-42.]

Antilarval measures are essential in the prevention of malaria on rubber estates.

The opening up of rubber estates in the malarious jungle of southern Indo-China and the importation of labour from non-malarious districts were followed by disastrous outbreaks. When prophylactic quinine and antilarval measures were applied in combination, amelioration soon followed, but where reliance was placed upon quinine alone conditions often became worse; on some estates, one-fifth of the coolies died in

the course of a few months, and the estates were perforce abandoned. On many estates, however, though no antilarval work was done things gradually improved, the daily turn-out of labourers was better, there were fewer sick and fewer deaths, and, after about 5 years, some places appeared to have become healthy without any expenditure on antilarval measures. The introduction of fresh, unsalted labourers into such an estate is always followed by an outbreak of malaria; which shows that the place is still malarious and that the reason why the old labour does not suffer is because it has become tolerant or immune. The children on such an estate, who too may be considered as newcomers, also suffer severely. Labour will never remain contented on an estate where nearly all their children die, and this will make things very difficult when contract labour is abolished, and it becomes necessary to import "free" labour.

The history of malaria on the plantations of Cochin-China and Cambodia has shown that antilarval measures must take the first place in prevention.

W. F.

MONIER (H. M.), GUY (R.) & ROS (M.). Renseignements sur le paludisme recueillis dans les régions de Luang-Prabang et Paklay, au Laos. [**Malaria at Luang-Prabang and Paklay in Laos.**—*Ann. de Méd. et de Pharm. Colon.* 1934. July-Aug.-Sept. Vol. 32. No. 3. pp. 309-327.

Luang-Prabang, the capital of the Kingdom of the Million Elephants and the White Parasol, is a pretty little town situated in the valley of the Mekong River, 6,500 feet above sea level. It is surrounded by jungle and contains innumerable sacred lakes. About a quarter of the cases treated at the hospital are due to malaria. The splenic rate determined by the authors was 16 per cent. in the centre of the town, but it was much higher on the outskirts, where it reached 78 per cent. in some districts. The parasitic index was 38 in this malarious area; in the centre of the town it was only 5.76.

Paklay is situated on the Mekong below Luang-Prabang, and contains a large native population because it is an important place on the caravan route between Laos, Siam and Burma. The town is traversed by innumerable small streams which run into the Mekong. They serve as breeding places in the wet weather; in the dry weather they dry up, but breeding continues in pools on the sandbanks uncovered by the shrinking river. The splenic index in children under 15 is about 50 per cent., and the parasitic index about 15. *P. vivax* constituted 76 per cent. of the infections. This is the reverse of what is found in the hospitals where 96 per cent. of the malaria cases are due to *P. falciparum*. The reason for this is that many of the people infected with *P. vivax* have no symptoms and therefore they do not go into hospital, *P. malariae* was found almost exclusively in children between 3 and 15 years of age, and *P. falciparum* in children over 15.

W. F.

RUSSELL (Paul F.). **Malaria and its Control in the Philippines.**—Reprinted from *Sugar News*. 1934. Nov. Vol. 15. No. 11. 6 pp.

An important paper. The local cultivation of cinchona and the manufacture of totaquina is advocated. This is a popular exposition of the causes and prevention of malaria in the Philippines which

contains many interesting facts and expressions of the author's opinions.

Malaria is serious and widespread in the Philippines; one may safely estimate that it kills from 10,000 to 20,000 Filipinos annually; there are probably two million cases a year throughout the islands, but in the cities of Manila, Cebu and Iloilo there is little or no malaria. There are only two carriers, and both of them breed in running water; they are:—*A. minimus* var. *flavirostris* and *A. maculatus*. The small streams at the foot-hills are the home of these mosquitoes; the lowlands, and the highlands above 2,000 feet, are not malarious.

Relatively few of the Filipinos can afford suitable treatment with quinine, but recent co-operative studies by the Bureau of Science, Forestry and Prisons, together with the Rockefeller Foundation, have shown that an excellent totaquina could be made in the Philippines to sell at about one-seventh of the price of quinine and yet to yield good profits to the grower, the manufacturer and the retailer. "There is a potential market in the Philippines alone for some 33 tons of this totaquina annually, without competing at all with the quinine and synthetic products now imported . . . totaquina is less bitter than quinine, has no bad effects and is equally efficacious. Totaquina would meet the need for an effective but much cheaper remedy. Furthermore, there would be a market for this totaquina in South China and it is possible . . . in the United States." W. F.

RUSSELL (Paul F.). **Malaria and Anopheles Reconnaissance in the Philippines, II.**—*Philippine Jl. Sci.* 1934. May. Vol. 54. No. 1. pp. 43-59. With 2 figs. on 1 plate.

Extended observations have confirmed the author's conclusions published in an earlier paper (this *Bulletin*, Vol. 30, p. 462). A list is given of 27 species of anophelines found in the Philippines. *A. minimus* var. *flavirostris* and *A. barbirostris* are the most common. *A. barbirostris* has never been found infected, but *A. minimus* is the most important carrier in the country. The *funestus-minimus* subgroup has been greatly confused in the past; it seems likely that *A. minimus* var. *flavirostris* has included *A. funestus*, *A. minimus*, *A. filipinae* and *A. mangyanus*. *A. littoralis* King ("salt-water *ludlowi*") and *A. ludlowi* Theobald ("fresh-water *ludlowi*") are not associated with malaria in the Philippines. It appears that certain larvae which were hitherto called *A. umbrosus* are really *A. baezai*, Gater. Malaria is widespread throughout the Philippine Archipelago; it is primarily a disease of the foothill regions, being found wherever there are streams containing larvae of *A. minimus*. The littoral when flat, the inland plains, and the mountains above 2,000 feet are not malarious. W. F.

RUSSELL (Paul F.). **The Small Spleen in Malaria Surveys.**—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 11-32. With 1 fig. [20 refs.]

A splenic index of over 5 per cent. denotes malaria.

Not more than 5 per cent. of children in non-malarious areas, have a "palpable-on-inspiration spleen." In the author's experience 45.5 per cent. of the children with such spleens have parasites in their blood; he finds that the more malarious a community, the more numerous are the p-o-i spleens. An incidence of over 5 per cent. suggests either:

(1) A community malarious at the time of examination, in which case the total spleen index will be in excess of 10 per cent. (2) A community where malaria has occurred, but where no transmission is taking place at present. In this case the index will be between 5 and 10. (3) A non-malarious community into which children have recently come from a malarious district. Tuberculosis does not enlarge the spleen sufficiently to vitiate the index. About 15 per cent. of scarlet fever cases have a residual palpable spleen which may last for several years.

W. F.

TREILLARD (M.). Une modalité de la zoophilie anophélienne en Indochine méridionale : *Neocellia fuliginosa* à la station d'altitude de Dalat (Annam). Points de vue biologique et antipaludique. [*Anopheline Zoophilism in Southern Indochina.*]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 754–756. With 4 figs. on 2 plates.

The author has studied the habits of *Neocellia fuliginosa* at the hill-station of Dalat in Annam. The inhabitants stop up every cranny in the walls of their houses at night because of the cold, but the cattle sheds which surround these houses are not built so carefully, nor are they hermetically sealed at night. Large numbers of *N. fuliginosa* are found in the cattle sheds, but none are found in the houses. This mosquito is a carrier in Burma, the Dutch Indies and British Malaya ; the author has infected it experimentally in Annam, but here it appears to have been deviated from man and to feed on animals. He considers it important that the existing equilibrium should be maintained by keeping animals in the neighbourhood of human dwelling places. He has found *N. fuliginosa* in some new barracks, where there were no stables in the vicinity.

W. F.

GASCHEN (H.). Infection naturelle de *Anopheles hyrcanus* var. *sinensis* (Wied. 1928) et la transmission du paludisme au Tonkin. [*Natural Infection of Anopheles hyrcanus var. sinensis in Tonking.*]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. June–July. Vol. 12. No. 6. pp. 554–557. With 1 fig. [12 refs.]

A. sinensis is an important carrier in some countries such as the Dutch East Indies, while in others—British India for example—it has never been found infective. The author reports the sporozoite infection of a specimen caught in Tonking. He suggests that there may be different races of *A. sinensis*, some of which carry malaria and others which do not.

W. F.

GALLIARD (H.) & SAUTET (J.). *Anopheles sacharovi* Favr. (*elutus* Edw.) et *A. maculipennis* var. *labranchiae* dans leurs rapports avec le paludisme en Corse. [*Anopheles sacharovi* Favr. (*elutus* Edw.), and *A. maculipennis* var. *labranchiae* in Relation to the Malaria of Corsica.]—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 855–857.

No answer has been found to the question why some places on the coast of Corsica are so malarious and why others are healthy.

A. elutus is present in large numbers all along the coast, and it is also found in certain spots some kilometres from the sea. *A. maculipennis*

labranchiae is present in equal numbers in these places, and is also found in the valleys which run up into the hills. *A. maculipennis* var. *messeae* and var. *melanoon* are also present in small numbers.

The authors attempted to discover if the prevalence of malaria in certain districts was dependent upon the presence of certain varieties of *A. maculipennis*. No such relation appeared to exist; the anopheline fauna of places where malaria was severe was the same and as numerous as that of many other places which were healthy. The conditions as regards cattle were apparently identical in malarious and in healthy places. The answer to the question has not yet been found.

W. F.

BOYD (Mark F.) & STRATMAN-THOMAS (Warren K.). **The Comparative Susceptibility of *Anopheles quadrimaculatus* Say, and *Anopheles crucians* Wied. (Inland Variety) to the Parasites of Human Malaria.**—*Amer. J. Hyg.* 1934. July. Vol. 20. No. 1. pp. 247-257.

A. quadrimaculatus is the more susceptible to infection; *A. crucians* is relatively unimportant.

Both species are widely distributed in Florida, but while about 1 per cent. of *A. quadrimaculatus* has been found infected in nature, and in one instance nearly 4 per cent., the rate for *A. crucians* is only 0.2 per cent. The authors found that while *A. quadrimaculatus* fed greedily on man, *A. crucians* could only with difficulty be induced to do so. Both species were infected when they were fed on patients whose blood contained large numbers of benign tertian or subtertian gametocytes, but when these were scanty, only *A. quadrimaculatus* was infected. In quartan cases, nearly one-fourth of the *A. quadrimaculatus* became infected, but none of the *A. crucians*.

W. F.

PECORI (G.) & ESCALAR (G.). **Relazione sulla campagna antimalarica nell' Agro Romano durante l'anno 1933. [The Antimalarial Campaign in the Agro Romano in 1933.]**—*Riv. di Malariaologia.* Sez. I. 1934. Vol. 13. No. 5. pp. 623-668. With 2 graphs & 1 map. English summary.

Malaria was much less severe in 1933 than in previous years. The inhabitants of the controlled area numbered 74,595. The malaria morbidity was 1.98 per cent. Only one death from malaria and one from blackwater occurred during the year. The splenic index of 7,299 school children was 4.6 per cent. The parasite index was 0.87 per cent. "A part of the Roman Suburbs and the Agro had been annexed to the territory of Rome City, and with a Royal Decree (8th May 1933) the entire Suburbs of Rome and the 'Lido' with Castel Fusano Park were declared free from malaria."

W. F.

BOYD (Mark F.), STRATMAN-THOMAS (Warren K.) & MUENCH (Hugo). **Studies on Benign Tertian Malaria. 6. On Heterologous Tolerance.**—*Amer. J. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 482-487.

An attack of malaria establishes some degree of tolerance of infections with heterologous strains. This tolerance is not sufficiently great to deal with a heterologous strain as efficiently as it can with the homologous strain, but it is capable nevertheless of diminishing the severity

of the heterologous illness. The authors reached this conclusion as the result of observations made on two groups of persons submitted to therapeutic inoculation with malaria. The first group contained people who had previously suffered from malaria, the second group contained people who had not. In the first group, the incubation period was longer, the fever was lower, and the loss of haemoglobin (from the beginning to the end of a 30-day period) was less. The same held good in a small group inoculated first with one strain, and then with another after they had recovered from the effects of the first. *W. F.*

BOYD (Mark F.) & STRATMAN-THOMAS (Warren K.). **Studies on Benign Tertian Malaria. 7. Some Observations on Inoculation and Onset.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 488-495

SCHAUDINN's statement that sporozoites enter erythrocytes is disputed.

Excision of the bite a few minutes after the application of an infected mosquito did not prevent infection, and the authors conclude that sporozoites must therefore be injected directly into the blood-stream.

Sporozoites can gain access to the blood vessels by penetrating the tissue, as was shown by applying infected mosquitoes to a blister raised by cantharides.

SCHAUDINN stated that he had observed the entry of sporozoites into erythrocytes, and their transformation into trophozoites. This observation has never been confirmed. A patient, "B," under the authors' care, was bitten by 15 heavily infected mosquitoes; on the same day and on each of the succeeding 9 days 10 cc. of his blood was inoculated into a series of susceptible persons. None of the series inoculated before the 9th day became infected, those inoculated on the 9th, 10th and 11th days became infected, and parasites appeared in the blood of patient "B" himself on the 11th day. "Despite the heavy inoculation given patient 'B,' parasites . . . could not be detected earlier than the 8th day following inoculation. This does not support the view that sporozoites invade the erythrocytes and thus directly initiate schizogony."

It is sometimes desirable to distinguish between a primary attack of malaria and a recurrence. In areas of low endemicity, the authors have found that the onset of a recurrence is distinguished from the onset of a primary attack by a greater number of parasites and a palpable spleen, but, where there is a great deal of malaria and more than one strain of parasites, these criteria are not very helpful. As regards the onset of the attack: in 37 per cent. parasites were found before the fever; in 37 per cent. fever occurred before the parasites, and in 26 per cent. both parasites and fever appeared on the same day.

W. F.

HELPERN (Milton). **Epidemic of Fatal Estivo-Autumnal Malaria among Drug Addicts in New York City transmitted by Common Use of Hypodermic Syringe.**—*Amer. Jl. Surgery.* 1934. Oct. Vol. 26. No. 1. pp. 111-123, 142. With 6 figs. [26 refs.]

During the five months from September 25, 1933, to February 28, 1934, there occurred in New York 49 cases of malaria among drug addicts who were intravenous injectors of heroin; 39 were subtertian infections, 21 of which were fatal; 9 were quartan, 1 of which was fatal;

I was benign tertian. At this time of year malaria does not ordinarily occur and anopheles are almost non-existent in Manhattan, the district in which the men lived. It was found on enquiry that the infection had been transmitted by the hypodermic syringe which was commonly shared by several addicts. A photograph of the "works" is given; this includes the improvised syringe and the bottle-cap in which the solution was prepared. Other photographs show sections of the cerebral cortex from a fatal case, with dilated capillary vessels containing red blood cells heavily infected with parasites. [See this *Bulletin* p. 109 above for references.] W. F.

SAUTET (J.) & CORDOLIANI (S.). Fièvre ondulante et paludisme. Difficulté du diagnostic au moment des poussées épidémiques. [The Diagnosis between Undulant Fever and Malaria.]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 719-723.

Undulant fever and malaria are both endemic in Corsica, and the spring epidemic of undulant fever coincides with the spring epidemic of benign tertian. The following points are of assistance in making a diagnosis: malaria is commoner in young children, undulant fever is commoner in adults; undulant fever may occur anywhere, malaria is limited to certain parts of the island; undulant fever does not react to quinine, malaria does react. The examination of blood-films and sera is the only means of making a sound diagnosis. W. F.

i. MÜHLENS (Peter). ii. SCHLESINGER (Wilhelm). Kommen heute noch Kriegsmalariafolgen vor? [Are the Sequelae of War Malaria still Occurring?]*—Arch. f. Schiffs- u. Trop. Hyg.* 1935. Feb. Vol. 39. No. 2. pp. 74-76. *Wien. Klin. Woch* 1935. Mar. 22. Vol. 48. No. 12. p. 365.

i. After reference to numerous diagnoses of war malaria, and deaths in consequence, which have been reported in the last two years in Germany the author notes that in such cases examined during the last 6-8 years at the Hamburg Tropical Institute malarial parasites have not in one single instance been found even after provocative methods and the like. Such reports should be critically received and no case accepted as malaria unless the parasites have been identified or confirmed, or in the case of death the organs examined by a competent person. He wishes such material sent to the Tropical Institute at Hamburg.

ii. From time to time Schlesinger gets war patients complaining of rigor with fever and terminal sweating but in the last ten years he has never found malarial parasites nor pigment in the blood nor mononucleosis, nor appreciable splenic enlargement. In 1920, in the great epidemic of influenza, he noticed that old malarials with pneumonia responded with intermittent fever though parasites were not demonstrable. He suggests that in these instances the heat centre has become adapted to that type of response and so would explain the rigors of his war patients, which have thus no special significance. A. G. B.

ALBERTO VIDELA (Carlos). Reactivación del paludismo latente por el cloruro de calcio. [Reactivation of Latent Malaria by Calcium Chloride.]—*Prensa Méd. Argentina.* 1934. Dec. 12. Vol. 21. No. 50. pp. 2378-2380. [13 refs.]

The author compares the provocative effect of berberine sulphate, adrenalin, and chloride of calcium in latent malaria. He tested these on 20 subjects infected with simple or double tertian and simple quartan

malaria. The berberine salt given by mouth was ineffective in three cases, and, intravenously, failed in another three. Adrenalin injected intramuscularly for several days in a dose of $\frac{1}{2}$ to 1 cc. of a 1/1,000 solution failed in 11 cases. Chloride of calcium, daily doses 10 cc. of a 10 per cent. solution intravenously, gave a positive result in four of the six patients in whom the other drugs had failed. The parasites appeared by the second or third day, and this reappearance coincided with a positive Henry's ferroflocculation and enlargement of the spleen [see this *Bulletin*, Vol. 28, p. 595].

H. H. S.

MANSON-BAHR (Philip). **The Prognosis in Malaria Infection.**—*Lancet*. 1934. Dec. 1. pp. 1237-1238.

Relapses in subtertian malaria can be entirely prevented by atebirin.

This excellent article should be read in full ; only a few points can be dealt with here. Dr. Manson-Bahr holds the view of most workers in the tropics that "In all forms of malaria, as in other protozoal infections, the earlier and the more energetic the treatment, the greater the hope of effecting a permanent cure." Not everyone will agree with him when he says "Apart from its disagreeable habit of manifesting relapses at odd and often unexpected intervals, benign tertian malaria cannot in any sense be regarded as a menace to life." He puts the life span of the benign tertian parasite at 3 or, at the most, $3\frac{1}{4}$ years, that of subtertian at about 9 months, and that of quartan at anything up to 5 or 6 years. He points out that the parasites of subtertian malaria have acquired the property of lying low and of springing into activity, precipitating sudden catastrophes, even death, by accumulating in the capillaries of the internal organs, so producing acute pancreatitis, dysentery, cerebral attacks, malarial amblyopia (a result of malarial infection of the retinal vessels) and many obscure symptoms. "These major and tragic aspects of subtertian malarial infections are more liable to be seen in the non-immune person—*i.e.*, the tenderfoot on his first visit to a malarious country."

Blackwater fever, on the contrary, seldom develops during a first infection ; the longer a person is infected, the more liable is he to develop it. It is the worst feature in the prognosis of subtertian malaria, for the mortality of the disease is about 25 per cent. It may appear at any time from the day of arrival in England up to 9 months after arrival, when the liability disappears. Attention is drawn to certain mental conditions which may resemble encephalitis lethargica, and "are produced by small subcortical haemorrhages which, if not immediately fatal, leave behind them disseminated malarial granulomata which represent the organization of the minute haemorrhages." The author considers that "it is now possible to exterminate this parasite [subtertian] in the blood with adequate doses of atebirin, with quinine perhaps as an adjunct, in a way never formerly anticipated ; it is possible to prevent entirely the recurrence of relapses." W. F.

DE SILVA (Stanley). **The Stroke in Malaria.**—*Jl. Trop. Med. & Hyg.* 1934. June 1. Vol. 37. No. 11. pp. 166-167.

A person who has once had cerebral malaria never has it again.

By "the stroke" the author means an attack of cerebral malaria with loss of consciousness, due to infection with malignant tertian parasites. He states that a patient with cerebral malaria either dies in coma, or

recovers and is free from further attacks of a similar nature. He himself has never met with a case in which there was a history of former "strokes," or in which subsequent strokes occurred. W. F.

VAN DER HORST (G. A.) & VERHAART (W. J. C.). Die Veränderungen im Gehirn bei Malaria. [**Cerebral Changes in Malaria.**—*Virchow's Arch. f. Path. Anat. u. Physiol.* 1934. Vol. 292. No. 4. pp. 417-427. With 4 figs. [43 refs.]

A study of the pathological anatomy of the brain in 21 cases of malaria in Batavia.

As a result of their investigations the authors found that the cases fell into different groups :—1. Cases with focal changes. 2. Cases with general changes and a few perivascular haemorrhages. 3. Cases with slight general changes, and 4. Cases without definite histological alteration of the brain, although pigment was present in the vessels. In the first group there were 8 cases and they all showed a lesion which was essentially the same as Dürck's granuloma ; it consisted of a perivascular necrosis surrounded by a number of microglial cells. This lesion is found in other diseases, and is, therefore, not specific for malaria.

From the investigation the authors conclude that pure malarial encephalopathy is extremely rare ; in 21 cases of malaria with cerebral changes it was only once found ; in the rest of the cases the clinical picture was obscured by cachexia, severe anaemia, jaundice and other complications ; it was the latter which caused death. Therefore the so-called malarial coma cannot be recognized as a special disease, the general intoxication playing the chief part. E. D. W. Greig.

RUGE (H.). Leberfunktion bei frischer Malaria. [**Liver Function in Acute Malaria.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Jan. Vol. 39. No. 1. pp. 14-19.

A study of the changes in the blood chemistry in a series of cases of acute malaria with a view to testing liver function.

The author notes that most liver function tests have been made in old and chronic cases of malaria. With the object of supplementing our knowledge he investigated two cases of natural malaria, two cases artificially infected by mosquitoes and nineteen cases of inoculated malaria, all showing acute symptoms and infected with *Plasmodium vivax*. The blood sugar was estimated after administration of 40 grams lactose.

As a result of his observations the author concludes that the disturbance of the liver function in acute malaria increases as the attack proceeds. The damage is shown by the rise of the blood sugar curve after administration of lactose to over 30 mgm. per cent., the increase of the nonprotein nitrogen, the occurrence of an indirect positive van den Bergh reaction. Under treatment with atebirin the changes in the blood chemistry returned to normal limits. E. D. W. Greig.

VAN NITSEN (R.). Quatre observations de paludisme congénital. [**Four Cases of Congenital Malaria.**—*Bull. Méd. du Katanga.* 1934. Vol. 11. No. 3. pp. 83, 85-87.

LAFFONT has proposed to limit the term "congenital malaria" to those cases where parasites are found at birth, and to designate as "hereditary malaria" the cases in which the infection is acquired during the delivery and where the parasites appear several days later.

Two of the author's cases come in the first category: in one, parasites were found in large numbers on the second day, and in the other on the third day. The other two cases were free from parasites until the tenth day.

W. F.

MOSHKOVSKY (S.) & POLIAKOVA (A.). Sur une méthode d'évaluation chimio-thérapeutique des propriétés schizotropes des préparations antipaludiques. [**A Method for Testing the Schizotropic Properties of Antimalarial Drugs in Chemotherapeutic Experiments.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 5. [In Russian pp. 395–400. French summary p. 400.]

The authors propose to test the "schizotropic" efficacy of anti-malarial drugs, *i.e.*, their damaging power upon schizonts, by determining the minimal single dose capable of producing an appreciable retardation in the course of the infection. This dose, named *dosis affectans*, differs from the "minimal effective dose" in that it does not lead to the disappearance—even temporary—of the parasites, but only lowers their growth-curve.

In determining this dose a number of birds (the authors employed linnets and siskins) are infected with equal quantities of parasites (*Plasmodium praecox*) capable of producing acute lethal infections without treatment. Those birds which show an equal percentage of infected erythrocytes at a given moment are selected for the comparative tests, for which atebirin and plasmochin were used. The minimal doses of these preparations producing the earliest diminution in the number of parasites constituted the *dosis affectans*. This proved to be between 0.2 and 0.3 mgm. per 20 gm. body-weight in the case of atebirin, and 0.03 to 0.04 mgm. for plasmochin. The ratio of D.A. of these two preparations corresponds more or less closely to that of their respective curative doses in human malaria. C. A. Hoare.

MOSHKOVSKY (S.) & BUROVA (L.). **Method of Evaluation of the Gametotropic Properties of Antimalarial Drugs.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 6. [In Russian pp. 445–451.]

The authors describe a method for testing the so-called "gamostatic" properties of anti-malarial drugs, *i.e.*, their inhibitory effect upon the sexual development of the malarial parasite, which renders it non-infective to the mosquito. The "gamostatic" effect manifests itself in an interruption of the process of microgamete formation and can be evaluated by observing the "exflagellation" of the parasites *in vitro*.

The tests were conducted with linnets and siskins experimentally infected with *Plasmodium relictum*, with linnets naturally infected with *Haemoproteus* and with human malarial parasites, using the following technique. Equal volumes of 1½ per cent. sodium citrate and infected blood are taken up in Pasteur's pipette and mixed on a slide. A small drop of the mixture is transferred to a fragment of cover-slip, measuring about 3–4 mm., over which a whole cover-slip is placed. This is mounted upon Ranvier's ring attached to a slide or over a hollow slide, with 1–2 drops of water at the bottom of the moist chamber, which is sealed with vaseline. Observations were made under a microscope placed together with the moist-chamber in a box kept at 28–30°C. Under these conditions exflagellation in *Haemoproteus*

occurred 3-8 minutes after the blood was taken, in *Plasmodium relictum* after 13-15 min. and in *P. falciparum* after 3-5 min. The effect of drugs upon exflagellation was tested with plasmochin, plasmocide, atebirin and quinine.

In the case of plasmochin and plasmocide a dose of 0.1 mgm. and 0.09-0.12 gm. respectively per 20 gm. of body weight, injected into birds infected with *Haemoproteus*, stopped exflagellation in 24 hours. On the other hand, 1 to 5 injections of 0.88 mgm. atebirin administered together with 2 mgm. of quinine per 20 gm. body-weight, had no effect upon the microgametes after 24 hours and more (only about 7 injections of atebirin inhibited exflagellation).

The experiments on *P. falciparum* were conducted with plasmocide and atebirin. The minimum dose of plasmocide producing cessation of exflagellation in 24 hours proved to be 0.09 gm. (given in three tablets on one day), while continued daily treatment up to 8 days caused the disappearance of the gametes from the blood. As in the case of bird-malaria, atebirin administered in doses of 0.12 gm. three times a day in the course of 5-8 days failed entirely to stop exflagellation. The authors recommend this method of testing the inhibitory effect of anti-malarial drugs upon exflagellation for general use in experimental chemotherapy of malaria.

C. A. Hoare.

KRITSCHESKI (I. L.) & DEMIDOWA (L. W.). Ueber eine noch unbekannte Funktion des retikuloendothelialen Systems. XXII. Ueber die Bedeutung des retikuloendothelialen Systems in der Therapie der Malaria. [**The Significance of the Reticuloendothelial System in the Treatment of Malaria.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Dec. 31. Vol. 84. No. 1. pp. 14-21. With 2 figs.

An investigation to determine the effect on the therapeutic activity of antimalarial drugs of blocking the reticuloendothelial system.

The drugs studied by the authors were quinine, plasmoquine, derivatives of acridine and acrichin No. 8. For the tests he employed birds infected experimentally with *Plasmodium praecox*. It was essential to determine very accurately the limit of the therapeutic dose of each drug for the birds. In one series of experiments the RES was blocked with trypan blue, in the other series the RES was intact. As a result of the investigation the authors reach the conclusion that the therapeutic activity of antimalarial drugs (quinine, plasmoquine, derivatives of acridine and acrichin No. 8) is greatly lowered by blocking the RES with trypan blue.

E. D. W. Greig.

QUARTERLY BULLETIN OF THE HEALTH ORGANISATION, LEAGUE OF NATIONS. Geneva. 1934. Sept. Vol. 3. No. 3. pp. 325-358. With 2 graphs.—**The Therapeutic Efficacy of Totaquina in Human Malaria. I. Clinical Tests carried out under the Auspices of the Malaria Commission** [PAMPANA (E. J.)]. **II. Critical Analysis of the Results Achieved** [FLETCHER (William)].

Totaquina acts like quinine as a potent remedy in all forms of malaria.

Tests of different samples of Totaquina (see this *Bulletin*, Vol. 29, p. 461, and p. 114, above) were carried out during the malaria season of 1933 in Algeria, Bulgaria, China, France, Italy, the Federated Malay States, Morocco, Rumania and Spain. Special cards for recording the

results were drawn up and sent to all the observers. The present report covers a total number of 1,144 cases, comprising 1,055 treated by totaquina and 89 treated by quinine as controls. Five samples of totaquina were used in these tests, they were as follows :—

Type I (made direct from the bark of *Cinchona succirubra*).

1. Made by Messrs. Burroughs & Wellcome.

2. „ Madras Government Factory.

Type II (made from residues of quinine extraction and adjusted to the Malaria Commission's standard specification).

3. Made by Turin State Quinine Factory.

4

5. Made by Messrs. Howards, London.

An analysis of these is given in the report. One of the Type II samples, number 4 above, resembled the Type I totaquinas in the proportions of the various alkaloids ; the other two, number 3 and 5, contained less quinine and more cinchonine, according to analyses made at the Wellcome Chemical Research Laboratories. The tablets of number 3 did not disintegrate very readily in water, because they were composed of pure totaquina without the addition of any substance to render them friable. Compressed tablets similarly manufactured, but made up with an excipient designed to render them friable, break up easily and can be kept for long periods under tropical conditions without special precautions.

A feature brought out by a study of the records was the difference in the condition of the patients at the beginning of treatment in one centre and in another. In some places the patients' symptoms were much more severe than in others. Another striking difference was the response of the patients to treatment : this was noticeably more prompt in the Rumanian centres than elsewhere. Neither the same samples of totaquina nor the same doses were used at all the different centres. This lack of uniformity would have mattered less if a control series had been treated with quinine at each centre ; unfortunately this was done only in Rumania and the Federated Malay States. As regards toxicity, the case records contained no cogent evidence that totaquina was more toxic than quinine in the doses given.

“ To sum up, the records of the cases treated at the different centres show clearly that Totaquina acts like quinine as a potent remedy in all forms of malaria ; but it must be remembered that a field trial of this kind is not a carefully controlled experiment and, when it comes to deciding whether Totaquina is a little better than quinine or not quite so good, one is on less sure ground and, in the absence of adequate controls treated with quinine, the yard-stick needed for more exact measurements is lacking. Similarly, the observations made at the different centres were not sufficiently precise and unanimous to warrant a final decision on the relative merits of the different samples of Totaquina.”

W. F.

SLATINEANU (A.), CIUCA (M.), BALTEANU (I.), ALEXA (E.), ALEXA (I.), FRANCKE (M.) & RUGINA (I.). Efficacité thérapeutique des alcaloïdes totaux de l'écorce de quinquina dans le paludisme humain (infection naturelle). [*The Efficacy of the Total Alkaloids of Quinine Bark.*—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 723-728.

From a study of 441 cases of malaria treated comparatively with different samples of totaquina and with quinine, the authors concluded that the samples used were as efficacious as quinine when the content

of crystallizable alkaloids and of quinine were the same as those of totaquina Type I; but that those Type II products in which the quinine was much less and the cinchonine much higher, were less efficacious unless given in larger doses. W. F.

CHOPRA (R. N.), ROY (A. C.) & GUPTA (B. M. Das). **On the Concentration of Quinine in the Blood after Intravenous and Intramuscular Injections.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 561–566. With 2 figs. [17 refs.]

There is little difference in the concentration of quinine no matter by what route it is administered. Parenteral injections should not be used for routine treatment.

Six monkeys were inoculated intravenously, and six intramuscularly, with quinine acid hydrobromide. The amount of quinine in the blood was estimated at intervals. The resulting average concentration of quinine in the blood was as follows:—

	Hours after injection of quinine.						
	$\frac{1}{4}$	$\frac{1}{2}$	1	2	4	5	24
Concentration after intravenous	1.37	1.27	1.05	0.63	0.35	0.36	0.00
Concentration after intramuscular	1.37	1.36	1.04	0.83	0.62	0.64	0.32

It is clear from this table that there is "not any marked difference in the concentration of quinine attained in the blood at different intervals of time when the effect of its administration by the two routes, *i.e.*, intravenous and intramuscular is compared." The maximum concentration in the blood was attained in 15 minutes by both methods. It has been stated that after intramuscular injection much of the quinine remains unabsorbed in the muscle. The authors investigated this in rabbits, and found that only small proportions remained unabsorbed after 20 hours. Four human patients were given quinine by the mouth, and also by intravenous and intramuscular inoculation.

The authors found that "if allowance is made for small variations due to the constantly changing factors in the animal organism, the concentration of quinine in the blood after administration by the oral and parenteral routes runs almost parallel. In some cases the concentration obtained within the first few hours after oral administration was definitely smaller, but the concentration soon rose to practically the level of the parenteral routes. . . . The oral route is undoubtedly the method of choice in the vast majority of patients . . . even in cases of severe malaria complicated with dysentery quinine has been shown to be absorbed . . . parenteral injection . . . should not be used for routine treatment of malaria, but is specially indicated in acute cases of severe type for as long as the emergency lasts." W. F.

MURPHY (R. A.). **Quinine in the Therapeutics of Malaria.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 566–567.

The author who has had many years' experience of the treatment of malaria in Assam pins his faith on a prolonged course of quinine. He

has been able to follow up his European patients for long periods. He treats the acute stage with 20 grains daily and then gives 10 grains a day for 3 months. The results in 110 cases were as follows :—cured, 80 ; relapsed, 20 ; unknown 10. Patients who had no fever for one year after treatment were counted as cured. He controls vomiting with adrenalin. He quarrels with the dictum of the Malaria Commission that, in relapses, it is safe to abstain for a day or two from giving a specific drug, and states that many a coolie child dies in convulsions just during these first few days of a relapse. [But it must be remembered that the Malaria Commission's report dealt with the subject "from the point of view of persons who are in a position to obtain expert medical advice and efficient care rather than from that of the mass of the population of malarious countries. The report does not contain information on plans for treating outpatients who attend at hospitals and dispensaries."]

W. F.

WILLIAMSON (H.) & SINGH (Shamsher). The Early Treatment of Malaria.—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 568–570.

The authors believe in intramuscular inoculations for the routine treatment of malaria (see CHOPRA, ROY and GUPTA above).

They have "recently been carrying out a series of experiments in treating a series of 600 cases of 'parasite positive' benign malaria"; and they conclude that "the dangers of intramuscular quinine have been exaggerated, and it is the best treatment for severe cases of benign malaria." Three hundred cases were given quinine by the mouth, 30 grains a day in a mixture; mag. sulph., calomel, and sodium bicarbonate being given as well. [Where these barbarous mixtures are used, patients will naturally do all they can to avoid taking them. As the authors say, "one great advantage of injected quinine is that the attendant knows that the patient is getting what the doctor ordered."] One hundred and fifty cases were given intramuscular injections. No untoward results followed and the pain "has never been so severe as that commonly felt after antityphoid inoculations." No less than 150 of the 600 benign tertian cases were treated with intravenous injections, 5 or 10 grains in 5 cc. of normal saline. A reaction occurred in about 30 per cent. of the patients; this consisted of rigors, collapse, vomiting and diarrhoea. One patient collapsed and died. Probably most people will agree with the authors that "it seems fair to assume that these reactions are due to the method and not to the drug." They naïvely quote a remark made by one of their colleagues in Quetta, "If I give an intravenous quinine I often find another doctor in attendance next time I go to see the patient." [Quinine, a gift of the gods, is loathed and feared; this is not difficult to understand.]

W. F.

SUBRAHMANYAM (S.). Intravenous Quinine Therapy in Malaria.—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. p. 570.

The author, who is attached to the Government Headquarters Hospital at Ootacamund had not had the alarming experience of WILLIAMSON and SHAMSER SINGH (see above), and he recommends intravenous injections for the routine treatment of malaria.

Since April 1932, about 300 cases of malaria of all types have been treated in the hospital, and the intravenous route has been almost invariably employed. The adult dose is 10 grains of the acid hydrochloride in 10 cc. of distilled water, and the injection is given once a day for 6 days. In patients with low blood-pressure, adrenalin is given at the same time. In cases where the blood-pressure begins to fall rapidly during the injection, or where there is respiratory embarrassment, the injection is stopped and is not repeated. In the majority of cases, there is a drop in the blood pressure of 5 to 15 mm. Hg., rarely 20 to 30 mm. The advantages of the treatment are: that it lasts only six days, it cuts short the primary attack, and it is at once cheap and effective. Almost every patient has complained of some giddiness and a slight burning sensation in the abdomen during the injection, but these are transient and need no treatment. In one or two instances, phlebitis has occurred, but it responded rapidly to treatment with two injections, intramuscularly on successive days, of 1 cc. of S.U.P. 36. Cyanosis and respiratory embarrassment were not observed, and the author concludes that "there does not seem to be any absolute contra-indication to the use of the drug intravenously." [It seems to the summarizer that to use intravenous quinine in every case of malaria is like using forceps in every case of labour.] W. F.

MANSON (D.). **Notes on Intravenous versus Intramuscular Quinine.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 571–572.

The author does not hold the views of SUBRAHMANYAM (see above) with regard to the safety of intravenous injections. The main drawback is shock following the injection. "However competently the injection is carried out, this does occur, and in cases already in the stage of collapse, the onset of shock is very sudden and little can be done to check the inevitable sequel." He uses the intramuscular route with ever increasing confidence, and, even in cerebral cases, is in doubt about the advantages of intravenous quinine. W. F.

MANCA (Serafino). La permeabilità della barriera nervosa centrale alla chinina. [**The Permeability of the "Central Nervous Barrier" to Quinine.**]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 5. pp. 601–609. French summary.

Quinine reaches the cerebrospinal fluid $\frac{1}{2}$ to 2 hours after administration.

The possibility of injected substances reaching the cerebrospinal fluid has been tested with a number of drugs—bromides, iodides, salicylates, arsenic, mercury, lead, morphine and several more—but, says the author, not the action of the "barrier" between the blood and the spinal fluid as regards quinine. For his experiments he used dogs and administered the drug intravenously, intramuscularly and orally. The usual doses were: for intravenous injection 20–25 cgm., for intramuscular 40–50 cgm., and *per os* 50 cgm. In all cases the quinine appeared in the cerebrospinal fluid after $\frac{1}{2}$ –2 hours according to the route of administration, quickest after the intravenous. The rate was enhanced if urotropine had been previously injected intravenously. Hence in severe forms of malaria, especially those with a cerebral symptom-complex, where circulatory disturbances obstruct the free

passage of quinine into the nervous system, the action of the drug can be assisted by preceding it with an intravenous injection of urotropine. Salicylate of sodium sometimes has the same effect as the urotropine.

H. H. S.

LOURIE (E. M.). **Studies on Chemotherapy in Bird Malaria. II.—Observations bearing on the Mode of Action of Quinine.**—*Ann. Trop. Med. & Parasit.* 1934. Oct. 19. Vol. 28. No. 3. pp. 255–277. With 4 figs. [13 refs.]

Quinine does not act upon the parasites by setting in action the mechanism of immunity ; it appears probable that it may act directly.

These experiments were made with a strain of *P. cathemerium* producing 16 merozoites every 24 hours. It was found that a very precise synchronicity of development and sporulation could be elicited by exposing infected canaries to light from 6 a.m. to 6 p.m., and confining them in a dark chamber from 6 p.m. to 6 a.m. Sporulation was then at a maximum at 4 p.m. every day. When an infection was checked by giving a dose of quinine at 4 a.m. there was a profound interference with the asexual reproductive cycle. Growth of the parasites was retarded, there was delay in reproduction so that the peak was reached at midnight instead of at 4 p.m. ; the number of merozoites was reduced from 16 to about 6, and the characteristic synchronicity of development was entirely lost. These effects of quinine treatment are in striking contrast to the checking of a superinfection by the immune substances present in a latently infected bird. In the latter case there is a much more rapid disappearance of the parasites, but reproduction continues to be synchronous, the cycle is not delayed, and the normal number of merozoites is produced. " It must be quite clear, then . . . that the therapeutic effects of quinine cannot be attributed to an activation . . . of the machinery which ordinarily comes to the service, eventually, of an untreated infected bird. . . . The mode of therapeutic action would seem rather to consist in an assault by quinine, or a derivative thereof, upon the parasite itself. . . . It is suggested that the fact of malaria parasites being able to retain their viability in the face of *in vitro* exposure to quinine in strong concentration is not a sufficient argument against the direct action of unaltered quinine *in vivo*."

The author attempted to determine *in vitro* the concentrations which so affected the parasites that on introduction into a bird they exhibited a delay in growth and reproduction similar to that which occurs when quinine is administered to the host. These experiments were hampered by the fact that delay occurred in the subsequent *in vivo* growth and sporulation in the parasites of the control blood which was incubated without quinine. It was found that the concentration of quinine required *in vitro* to cause a subsequent delay in sporulation still greater than that of the control parasites, incubated in absence of the drug, was about 1 : 5,000, after an exposure of 1 to 2 hours at 39°C. " It is extremely unlikely, in view of the findings of other workers, that such very strong concentrations could be maintained for any length of time in the blood stream." Nevertheless minute amounts of quinine remain in the circulation for many hours after a therapeutic dose, and these very small amounts may be able, during that time, to act directly upon the parasites. An attempt was made to demonstrate the presence

of quinine, or an active derivative, in the blood, spleen or liver of birds which had received large doses of quinine, but the result was negative. [For No. 1 of this series see above, p. 117.] W. F.

LOURIE (E. M.). **Studies on Chemotherapy in Bird Malaria. III.—Difference in Response to Quinine Treatment between Strains of *Plasmodium relictum* of Widely-Separated Geographical Origins.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 513-523. [12 refs.]

Different strains of bird malaria react differently to quinine.

The author demonstrates that in bird malaria response to quinine is liable to vary according to the particular distinct strain which may be under observation. Two strains of *P. relictum* were employed, one from America and the other from Germany. In the first series of experiments, canaries were inoculated with these strains and were treated with daily doses of quinine from the beginning. The quinine suppressed the infection in the canaries inoculated with the American strain, but it failed to do so in those infected with the German strain. Confirmation of these results was obtained in a second series of experiments where so large a dose of the infecting material was inoculated intravenously that parasites could be counted in the blood immediately afterwards. Quinine was given daily as before, with the result that the parasites of the American strain disappeared from the blood by the 10th day, but it had little or no effect upon the German strain. The two strains appeared to be of equal virulence; the American strain was not milder than the German; the difference was one of resistance to quinine. W. F.

FIELD (J. W.) & KANDIAH (M.). **A Note on the Use of Mayer's Reagent for the Detection of Quinine in Alkaline Urine.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 385-390. With 2 charts.

This is a further account of the work summarized in this *Bulletin* Vol. 31, p. 431, with reference to the failure of Mayer's reagent to precipitate quinine in alkaline solutions.

"We have now examined some thousands of specimens of urine for quinine using both Mayer's reagent and a modified Mayer's reagent containing acetic acid. For routine clinical use there has appeared little to choose between them. Their relative advantages and disadvantages have seemed to be as follows:—*Mayer's Reagent*: (1) Does not precipitate albumin within the normal clinical range of pH. (2) May fail to precipitate quinine from alkaline urine. *Acid Modification of Mayer's Reagent*: (1) Always precipitates albumin. (2) Always precipitates quinine if present in clinically significant amount. (3) Occasionally precipitates other substances. . . . While fully recognizing the limitations of any simple form of Mayer's test used in untreated urine, we believe the following procedures to be relatively free from fallacy:—

Using Mayer's Reagent:—

"(1) Add clear urine to each of two tubes.

"(2) To one tube add a few drops of glacial acetic acid.

"(3) To both tubes add a few drops of Mayer's reagent.

"i. If turbidity appears in both tubes, the presence of quinine is highly probable. Confirm by demonstrating the disappearance of the turbidity

on boiling the urine in the acid tube. If the turbidity does not disappear, albumin is probably also present. In this case, filter while hot to remove the albumin. The filtrate should be clear. Quinine, if present, will precipitate as the filtrate cools.

"ii. If both tubes remain clear, the presence of quinine at a concentration greater than 1/250,000 is highly improbable.

"iii. If the acid tube only shows turbidity, the presence of albumin, quinine, or both may be inferred. To identify quinine, boil and filter hot as in i."

W. F.

NEWMAN (C. D.) & CHALAM (B. S.). **Atebrin in the Treatment of Malaria in Railway Employees.**—*Indian Med. Gaz.* 1935. Jan. Vol. 70. No. 1. pp. 5-8.

Atebrin is less expensive than quinine.

The patients were employees and their dependants on the Eastern Bengal Railway; 258 were given three tablets of atebrin daily for 5 days, followed by three tablets of plasmoquine daily for a further period of five days. A second series of 76 persons were given the plasmoquine and atebrin together during a single period of five days. In the first group 5.8 per cent. exhibited untoward or toxic symptoms but in the second group 21 per cent. The parasites disappeared after a few days treatment. The cost of treatment was on the whole less than treatment with quinine. (A three weeks course of quinine was taken for comparison.)

W. F.

WILLIAMS (D. P.) & BHATTACHARYYA (Rasamay). **Notes on an Experiment on the Prophylactic and Curative Value of Atebrin and Plasmochin Therapy in a Tea Garden in Assam.**—*Indian Med. Gaz.* 1935. Jan. Vol. 70. No. 1. pp. 8-14.

Atebrin is more expensive than quinine.

"Atebrin is a more suitable drug for those who can afford it, but it cannot replace quinine in general use in a poor country like India."

The usual curative course of quinine on these tea gardens consists of 20 grains daily, for 7 days. The small reduction of malaria which followed prophylactic treatment with atebrin and plasmoquine was not sufficiently satisfactory to compensate for the expense incurred.

W. F.

KINGSBURY (A. Neave). **Psychoses in Cases of Malaria following Exhibition of Atebrin.**—*Lancet.* 1934. Nov. 3. pp. 979-982.

"Seven cases of psychosis following the exhibition of atebrin to cases of malaria have been collected. Five previously unpublished cases (McSwan) have been cited and five more cases are recorded. [There were apparently 12 cases in all, not 17.]

"These occurred among several thousand cases of malaria treated with atebrin. . . . The complication has been noted after a minimum of 6 tablets . . . a maximum of 21 tablets and an average of 13 tablets. The minimum interval between the commencement of treatment and the onset of symptoms was 1½ days, the maximum 12 days (5 days after the completion of the course) and the average 5½ days. The duration of symptoms in 8 mild cases varied from ½ to 7 days, with an average of 1½ days. Four more severe cases were referred to mental hospitals. . . . Two factors may be involved in the causation. The

action of atebtrin *vis-à-vis* the malarial parasite may result in an intense liberation of 'toxins': on the other hand, atebtrin (in lethal dosage) is known to have a toxic action on the central nervous system. Although the plasmodicidal effect of atebtrin in a daily dosage of 0.2 grams is less favourable than that obtained with a larger intake, it is suggested that the risk of the development of psychoses would be minimised by caution in the selection of the daily dose." Details of 6 cases are given and on reading these one wonders how much was due to atebtrin and how much was due to malaria. W. F.

DE LANGEN (C. D.) & STORM (C. J.). Experimenteel onderzoek van circulatiestoornissen door plasmochine en atebrine. [**Experimental Investigation of Circulatory Disturbances caused by Plasmoquine and Atebrin.**]*—Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Dec. 4. Vol. 74. No. 25. pp. 1646-1658. With 12 figs. [20 refs.]

Plasmoquine and atebtrin are circulatory depressants in monkeys.

Before putting out claims for the value of an antiparasitic medication it is necessary to examine carefully into contra-indications and complications. In particular, investigation of its organotropic effects is very desirable and the determination of its therapeutic index, which is the ratio between the smallest effective dose and the smallest lethal dose for the infected individual. An advantage which the worker in the tropics has over those of other lands is the ease with which he can use monkeys as experimental animals, for they are animals from which results can be directly transferred to man. That plasmoquine and atebtrin do affect the circulation adversely is apparent from their effect upon the blood pressure and the experiments recorded upon monkeys by the authors have reference to this as an index. Plasmoquine, in a quantity of 2 mgm. by intravenous injection (0.1 per cent. in physiological salt solution), causes on an average a fall of 500 mm. mercury and 1 cc. atebtrin (2 per cent. solution) a systolic and diastolic fall of 100 to 65 mm. and 75 to 50 mm. respectively. The experimental results are illustrated throughout by very clear curve tracings. Some of the conclusions drawn are:—1. Plasmoquine and atebtrin exert a depressing effect on the circulation in monkeys, especially by intravenous administration and cause disturbance of the respiration. These are only in part dependent on the speed of administration and the dilution. 2. It is possible then that intravenous injection, or a massive dose by the mouth, above all in malignant malaria where blood pressure is already low, may be followed by fatal collapse as well as by serious respiratory disturbance. 3. Adrenalin is recommended for intravenous injection along with plasmoquine and atebtrin, as being in many respects antagonistic to them. 4. Adrenalin by its action on organs like the spleen, that are innervated by the splanchnic nervous system, brings parasites out into the peripheral circulation and so promotes contact between them and the anti-parasitic drug. 5. It is advantageous from the point of view of circulatory complications to combine quinine not only with plasmoquine but also with atebtrin.*

W. F. Harvey.

* HUGHES finds that quinine given intravenously is a circulatory depressant and its administration not devoid of danger [this *Bulletin*, Vol. 28, p. 1006].—Ed.

CHOPRA (R. N.) & CHAUDHURI (R. N.). **Some Observations on the Toxicity of Synthetic Anti-Malarial Remedies.**—*Indian Med. Gaz.* 1935. Jan. Vol. 70. No. 1. pp. 1–5. [17 refs.]

Points of distinction between blackwater and plasmoquine poisoning are given. Plasmoquine and atebirin should not be given together.

The authors give the details of a number of cases of poisoning in cases where a combined treatment with atebirin and plasmoquine had been given. They consider that combination with atebirin enhances the toxicity of plasmoquine. They state that though plasmoquine poisoning resembles blackwater fever, oxyhaemoglobinuria and oxyhaemoglobinaemia are never the result of the former though they are present in blackwater. Another point of distinction is the presence of cyanosis in plasmoquine poisoning and its absence in blackwater. They conclude "that 0.02 gram plasmoquine daily for a 2 or, at most, a 3 days' course causes disappearance of the crescents in the peripheral blood in cases of Indian strains of malaria and prolonged use is unnecessary and dangerous. Neither plasmoquine nor atebirin should be used for prolonged periods for prophylactic purpose. Patients should not be allowed to use these drugs except under direct medical supervision."

W. F.

TATE (P.) & VINCENT (M.). **The Action of Atebrin on Bird Malaria.**—*Parasitology.* 1934. Oct. Vol. 26. No. 4. pp. 523–530. [13 refs.]

Atebrin does not act as a prophylactic in mosquito carried *P. relictum* infections in canaries.

The authors investigated the prophylactic action of atebirin in blood-inoculated, and in mosquito-induced, infections of *P. relictum* in canaries. They found that when the infection was conveyed by direct blood inoculation, atebirin acted as a clinical prophylactic and delayed the appearance of parasites; but when the infection was conveyed by mosquitoes it had no prophylactic action, whether it were given before or after the infective bites, though it diminished slightly the severity of the attack and the degree of splenic enlargement. In cases of infection by mosquitoes, parasites appeared in the blood during the course of atebirin treatment if this were prolonged beyond the normal incubation period. Asexual parasites which appeared in the blood of birds after atebirin treatment were devoid of pigment and stained badly. Atebrin treatment produced peculiar bodies in the blood cells of canaries.

W. F.

KRITSCHESKI (I. L.), MAGIDSON (O. J.), HALPERIN (E. P.) & GRIGOROWSKI (A. M.). **Die Synthese chemotherapeutischer Verbindungen. Akridinderivate gegen Malaria. [Synthetic Acridine Derivatives for the Treatment of Malaria.]**—*Giorn. di Batteriol. e Immunol.* 1934. Oct. Vol. 13. No. 4. pp. 685–700. English summary (9 lines).

The authors refer to the important investigations of KIKUTH on atebirin, an acridine derivative, in the treatment of malaria (see this *Bulletin*, Vol. 29, p. 705, and Vol. 30, pp. 198 and 480), and then describe their own observations on the subject.

They employed birds infected with *Plasmodium praecox* using the method of Kritschewski and STERNBERG for testing the therapeutic

activity of the drugs prepared by them. They studied in all nine acridine derivatives.

As a result of their investigations they found two acridine derivatives therapeutically active against malaria, namely, acrichin 5, which is the dichlorhydrate of the 2-methoxy-6-chloro-9-diethyl-amino-propyl-amino-acridine, and acrichin 8, which is the dichlorhydrate of the 2-methoxy-6-chloro-9-diethyl-amino-butyl-amino-acridine. The former has the same therapeutic index as atebirin and has the advantage of being easier to prepare. The latter has a higher index than atebirin and is also easier to prepare.

E. D. W. Greig.

KIKUTH (W.) & SCHÖNHÖFER (F.). Das Plasmochin und Atebrin. [**Plasmochin and Atebrin.**]*—Muench. Med. Woch.* 1935. Feb. 21. Vol. 82. No. 8. pp. 304-308. With 5 figs.

An interesting account of the origin, trial and introduction of these two valuable synthetic antimalarial drugs.

A. G. B.

MASSIAS (Ch.), BOURGIN (P.) & NGUYEN-VAN-TAN. Traitement du paludisme par un dérivé acridinique et un dérivé quinoléinique, nouvelles observations. [**The Treatment of Malaria with Acridine and Quinoline Derivatives.**]*—Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 929-932.

This concerns treatment with quinacrine followed immediately by a course of treatment with a mixture of rhodoquine and quinio-stovarsol known as stovoquine.

[Quinacrine is chloro-2-diethylamino-pentylamino-5-methoxy-7-acridine, or R.P.866; its action resembles that of atebirin (under which name it is now advertised); see this *Bulletin*, Vol. 31, p. 697.]

Rhodoquine is dichlorhydrate of diethylamino-propylamino-methoxyquinoline, or Fourneau 710; its action resembles that of plasmoquine; see this *Bulletin*, Vol. 30, pp. 479-850, and Vol. 31, p. 433. The name rhodoquine was formerly used for all the Fourneau quinoline derivatives, such as 574 and 915, it now indicates 710 only, the other products being distinguished by a letter following the name; for example 574 is rhodoquine U.]

The authors' treatment was as follows: quinacrine 0.3 gram daily for 5 days, followed by 0.03 gram of rhodoquine and 0.75 gram of quiniostovarsol daily for a further period of 5 days. The above dose of rhodoquine is intended for a man of 60 kilos; it should be calculated at the rate of 0.0005 gram per kilo of body weight. No toxic symptoms were produced by the treatment. The results as regards the disappearance of fever and parasites were excellent.

W. F.

CHORINE (V.). Mécanisme et application de la réaction de Henry. [**The Mechanism of Henry's Reaction.**]*—Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 6. pp. 807-822. With 2 figs. [48 refs.]

Flocculation with distilled water (surflocculance) and melano-flocculation are the same. Melano-flocculation is not due to specific antibodies.

Melano-flocculation, in therapeutic malaria, becomes positive about the third or fourth day after inoculation of the infection, and increases in intensity until the sixth or seventh malarial paroxysm. The

reaction becomes negative in one or two months under specific treatment. It disappears at the beginning of a paroxysm and returns as it passes off. The clinical value of the reaction is undeniable; a negative reaction means the absence of malaria, but a positive reaction is only presumptive evidence of its presence. The flocculation of the serum in distilled water follows a curve parallel to that of its flocculation with melanine; it increases with the malarial paroxysms, and it decreases under treatment in exactly the same way. The two flocculations are really the same, and the more simple reaction with distilled water, measured with the photometer, is to be preferred. Melano-flocculation is not due to specific antibodies; neither the pigment of an ox's eye, nor that of a melanotic sarcoma possess antigenic power. The reaction is due, in the main, to an increase in the euglobulins of the blood, helped to some extent by an augmentation of the cholesterine and uric acid. The reaction is inhibited by an increase in the molecular concentration of the blood, and its disappearance during the malarial paroxysm is due to a rise in the salt content. Serum albumins and pseudoglobulins also tend to suppress the reaction.

W. F.

TRENSZ (F.). Sur la nature des "fausses-flocculations" en sérologie palustre. [**Henry's Reaction and the Nature of False Flocculation.**]*—C. R. Soc. Biol.* 1934. Vol. 117. No. 37. pp. 1106–1107.

Flocculation depends upon chemico-physical changes connected with the euglobulins.

Melano-flocculation occurs in several diseases in addition to malaria; for example, it occurs sometimes in tuberculosis, syphilis, cirrhosis of the liver and anaemia, and in experimental trypanosomiasis it is very common; in typhus exanthematicus and in the spirochaetosis of fowls it is almost always positive. HENRY maintains that his melano-flocculation is a specific reaction due to the pigment antibodies. He considers that the flocculations which occur in these other diseases, where no pigment is produced, are of a different nature from those which occur in malaria, and he calls them "false flocculations." He has published a method by which, he claims, these "false flocculations" can be distinguished from the flocculations seen in malaria. (See above, p. 132.)

The author has employed this technique in the examination of 18 animals infected with trypanosomiasis, with the result that 4 were positive, 3 were doubtful, and 11 negative. These flocculations were therefore true flocculations. He concludes that there is no difference except in degree between the flocculation occurring in malaria and that occurring in other diseases, and that the phenomenon of flocculation depends upon physico-chemical change connected with the euglobulins of the serum.

W. F.

TRENSZ (F.). Sur les caractères distinctifs entre la "flocculation" et la "surflocculation" du sérum des paludéens. [**Henry's Reaction. The Distinction between Flocculation and Surflocculation.**]*—C. R. Soc. Biol.* 1935. Vol. 118. No. 1. pp. 11–12.

The author considers that the two phenomena are distinct from one another.

Surflocculation is due to the reaction which takes place between the euglobulins of the serum and distilled water ; flocculation is due to the reaction of these same euglobulins with melanine. If the melanine reaction is carried out in 0.3 per cent. ammonium chloride instead of water, surflocculation is suppressed while flocculation with melanine remains. (See Chorine below.) W. F.

CHORINE (V.). Flocculation du sérum dans l'eau distillée pure ou additionnée de mélanine. [**Henry's Reaction. Flocculation with Melanine, and in Distilled Water.**].—*C. R. Soc. Biol.* 1935. Vol. 118. No. 4. pp. 335–338. With 1 fig.

Melanine is merely an indicator, not an antigen.

TRENSZ (see above) states that surflocculation in distilled water and flocculation with melanine are distinct phenomena, and that surflocculation can be abolished by the addition of ammonium sulphate while flocculation with melanine remains unaffected. The author has plotted out curves of flocculation with melanine and with distilled water, as measured with the photometer, in different strengths of ammonium sulphate ranging from 1 to 10 per cent. The molecular salt diminishes the flocculation in both series, until, with increasing concentration, it is suppressed. The degree of flocculation in the melanine series is higher than in the distilled water series, and, consequently, visible flocculation disappears first in the latter (on the addition of about 3 per cent. ammonium sulphate); but the two curves are almost exactly parallel, and it is clear that melanine acts solely as an indicator. HENRY employs sodium chloride in the same way as TRENSZ employs ammonium sulphate. W. F.

CASTRONUOVO (G.) & GERACITANO (A.). Le melanine e l'emozoina malarica. [**Melanin and Malarial Haemozoin.**].—*Riforma Med.* 1934. Dec. 1. Vol. 50. No. 48. pp. 1841–1845. With 3 figs. [14 refs.]

[This article is, at present at all events, mainly of academic interest.] By using the polarizing microscope the authors find that malarial pigment is not melanin. Melanin, they state, has its primary source in the nucleus of a cell and is the product of complex metabolic processes, katabolic and synthetic. In any case melanin is formed within the cell at the expense of protein derivatives and it is probable that its production is the result of the processes of condensation and oxidation due to complex enzyme action. Malarial pigment on the other hand is shown by crossed Nicol's prisms to be a substance of a crystalline nature which retains its doubly refractile characters after treatment with alcohol and fatty solvents and hence is not of a lipid nature.

H. H. S.

GHOSH (B. N.) & NATH (M. C.). **The Chemical Composition of Malaria Pigment (Haemozoin).**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 321–325.

"Haemozoin from blood heavily infected with *P. knowlesi* has been purified and subjected to a quantitative chemical analysis by micro-methods. Its carbon, hydrogen, and iron contents agree with those of haematin ; but compared with the latter pigment, the amount of nitrogen was found too low. This has been attributed to experimental error."

W. F.

FRÖES (H. P.). Il "blu di metilene" nella diagnosi della malaria. [**Methylene Blue in the Diagnosis of Malaria.**—*Riv. di Malarologia*. 1934. Vol. 13. No. 4. pp. 481–483. English summary (5 lines).

The author recommends the staining of thick films with an acid solution of methylene blue (methylene blue 1 gm., hydrochloric acid 0.5 cc., distilled water 90 cc., 90 per cent. alcohol 10 cc.). The stain is applied directly to the dry film and allowed to act 1–2 minutes, after which the slide is carefully washed in water till the film has a greenish-yellow colour.

H. H. S.

EATON (Paul). **Susceptibility of Red Cells to Malaria. A Preliminary Note.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 431–437. With 1 fig.

The author proposes the hypothesis that the red cell is susceptible to infection with malaria only when it is in the reticulocyte stage. He describes a method for staining reticulocytes.

The nucleus of the normoblast is extruded at the moment when the red cell is cast into the circulation. A network of fibrils which previously surrounded the nucleus remains for a short time, and, as this dissolves in the cytoplasm, the remaining fragments are drawn up into small spherical drops. The simplest method of staining these young cells, or reticulocytes, is to make a blood film on a slide which has been coated with a very thin film of brilliant cresyl blue. The serum dissolves the dye, the cells take it up while they are still alive, and the reticulum stains more deeply than the rest of the cell. The films may then be stained with Leishman's or Giemsa's stain. The average red cell lives about 30 days; thus about 1/30 are destroyed and replaced by new cells every day. This means that 1/60 of the whole number of red cells (roughly 1.5 per cent.) are less than 12 hours old. The reticulocyte stage lasts about 12 hours, and it follows that the average percentage of reticulocytes in health is about 1.5. The author suggests that the infection of red cells occurs when they are in the reticulocyte stage. In a case of therapeutic benign tertian, 23 per cent. of the reticulocytes, and only 1.8 of the adult cells, contained parasites. In twenty additional preparations made from 4 cases, the percentage of infected reticulocytes ranged from 20 to 50.

W. F.

DENECKE (K.) & MALAMOS (B.). Ueber das makrozytäre Blutbild bei der Malaria. [**Macrocytic Blood Picture in Malaria.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Feb. Vol. 39. No. 2. pp. 51–63. With 5 figs. [40 refs.]

A haematological study of cases of human and monkey malaria to determine if there is a macrocytosis of the red cells.

The authors conclude as a result of the investigation that 16 out of 24 cases of malignant tertian, and 6 out of 8 benign tertian, cases showed a macrocytosis (average diameter of red cells from 8.03 to 8.81 microns). The patients had a slight anaemia, as a rule, but at times the haemoglobin and red cell values were normal; marked anaemia was present in only one case. In monkeys infected with *Plasmodium knowlesi* an early macrocytosis occurred which could not be attributed only to a flooding with young large cells from the marrow. Eleven patients tested for liver

function showed that the liver efficiency was lowered, and this they considered as a possible cause of the macrocytosis. The blood picture was an early macrocytosis and never a megalocytosis. Bearing in mind this distinction between the red cells, it is possible that a proportion of the macrocytic red cells were not young marrow cells, which had been washed out, but red cells in the peripheral blood which had been altered in form by the action of toxic substances. *E. D. W. Greig.*

LOWE (John). **Studies in Untreated Malaria. Numerical Studies of the Parasites in Relation to the Fever.**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 223-241. [19 refs.]

The relation of the numbers of parasites to the course of the fever is not the same in benign tertian and subtertian.

The parasite counts made by the author ranged from 20 to 202,000 per cubic millimetre. The highest recorded count found by him in the "literature" was one of 2,800,000 reported by CHOPRA, Das GUPTA and SEN in a fatal case of subtertian.

In benign tertian malaria :—(a) A minimum count of 500 parasites per cmm. is usually necessary to cause fever, but this differs in different patients. (b) The variations in the numbers in a given patient are not due to migration of the mature parasites to the internal organs, but to their multiplication and destruction. (c) The schizont count, before a rigor, was compared with the young trophozoite count after the rigor. The largest increase in parasites was a ninefold one. Usually the increase is much less than this, because many of the merozoites—50 to 100 per cent.—fail to infect red cells and are destroyed. (d) On an average, only some 20 per cent. of the young trophozoites reach maturity, as was shown by counting them just after a rigor, and comparing the figure thus obtained with the number of schizonts present about 40 hours later.

In subtertian malaria :—(a) A count of 600 to 1,500 parasites is usually necessary to cause fever. (b) The wide and frequent fluctuations in their number is ascribed to the migration of mature parasites to the internal organs, and to the flooding of the blood with young parasites which come from these organs. (c) Increase or decrease in the parasite count is not necessarily followed by an increase or decrease in the fever of subtertian malaria, but, in benign tertian, the fever generally rises and falls with the number of parasites. The author considers that the destruction of parasites occurs in two ways: (1) by lysis or phagocytosis of free merozoites. (2) By ingestion of infected red cells by the reticulo-endothelial system. *W. F.*

TATE (P.) & VINCENT (M.). **The Susceptibility of Autogenous and Anautogenous Races of *Culex pipiens* to Infection with Avian Malaria (*Plasmodium relictum*).**—*Parasitology.* 1934. Oct. Vol. 26. No. 4. pp. 512-522. [18 refs.]

Two strains of the same species of avian malaria may produce very different infection rates in mosquitoes, and this difference is not merely one of the relative numbers of gametocytes formed by different strains.

An Algerian strain of *P. relictum* produced an infection rate of 89 per cent., while with a German strain the rate was only 43 per cent. The difference in the infection rates does not depend upon the strain of *C. pipiens* which is employed as a vector. A given strain of *P.*

relictum was transmitted to the same proportion of birds, by English, Greek, Maltese, Hungarian or cross-bred strains of *C. pipiens*. Some birds resisted infection with the sporozoites of *P. relictum*, and a few (less than 1 per cent.) resisted infection by blood inoculation. No seasonal influence was found as regards the infection of *C. pipiens* by *P. relictum*.
W. F.

SHAH (K. S.), ROZEBOOM (L. E.) & DEL ROSARIO (F.). **Studies on the Infectivity of *Plasmodium cathemerium* of Canaries for Mosquitoes.**—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 502–507.

Gametocytes and infectivity appear as early as trophozoites. Some individual mosquitoes are immune.

Canaries, *Culex pipiens* and *P. cathemerium*, were used in these experiments. It was found that when mosquitoes were fed on canaries during the early course of infection, some of them became infected during the first and second day on which parasites were present in the blood, but the percentage of infection was low. Individual immunity existed among mosquitoes; when a batch of mosquitoes all ingested the same number of parasites, some of them resisted infection, provided the number was not too great; when enormous numbers of parasites were ingested this individual resistance was broken down and all the mosquitoes became infected. It was found that mosquitoes feeding during the night were more likely to become infected than those feeding during the day, and the authors attribute this to the presence at night of a greater number of mature gametocytes in the blood. In infections of canaries, both with injections of blood containing asexual forms and with injections of sporozoites, gametocytes were produced early in the infection, and in most cases simultaneously with the appearance of asexual forms.
W. F.

- i. TALIAFERRO (William H.) & TALIAFERRO (Lucy Graves). **Morphology, Periodicity and Course of Infection of *Plasmodium brasilianum* in Panamanian Monkeys.**—*Amer. Jl. Hyg.* 1934. July. Vol. 20. No. 1. pp. 1–49. With 17 text figs. & 85 figs. on 2 plates. [21 refs.]
- ii. — & —. **Alteration in the Time of Sporulation of *Plasmodium brasilianum* in Monkeys by Reversal of Light and Dark.**—*Ibid.* pp. 50–59. With 3 figs.
- iii. — & —. **Superinfection and Protective Experiments with *Plasmodium brasilianum* in Monkeys.**—*Ibid.* pp. 60–72. With 2 figs. [15 refs.]

This investigation follows similar work on the infection of *P. cathemerium* in the canary (this *Bulletin*, Vol. 28, p. 494).

i. *Plasmodium brasilianum* was studied in 9 naturally infected and 67 experimentally infected Panamanian monkeys. These comprised black and red spider-monkeys, black and brown howlers, white-throats, marmosets and night monkeys. The sexual and asexual stages of the parasite are uniformly quartan-like. They do not enlarge the red cell. The asexual cycle exhibits a 72-hour quartan periodicity, and sporulation occurs regularly between 8 a.m. and 4 p.m. on every third day if one brood of parasites is present, but in natural infections there are often several broods in the blood. The mean number of nuclei occurring in sporulating forms varies between 8.5 and 10. The morphology of the parasite shows slight differences in the different

species of monkeys ; in some, band forms are noticeably common ; in others, the number of nuclei in the schizonts is above the average. Moreover, the disease is more severe in some species than in others. The infections are characterized by (1) an acute rise in the number of parasites ; (2) a crisis with a fall in their number, either precipitous or gradual ; (3) a developed infection which is of low grade ; (4) a series of short latent-periods, when no parasites can be found, alternating with relapses. The relapsing nature of the infection corresponds to that of quartan malaria in man. Without any mortality of parasites, the infections should increase by about 9 times at each sporulation, since the number of merozoites produced is 8.5 to 10 for each schizont ; but even during the acute rise, the greatest increase is far less than this. After the survivors successfully enter new cells, more perish during the acute rise, but an even greater mortality takes place at the crisis and thereafter.

"The death of the parasites before the crisis takes place in a previously uninfected host and represents natural resistance, that at and following the crisis is increased as a result of infection and represents acquired resistance." The authors found no difference between primary attacks and relapses ; in both, the temperature was correlated with the growth of the parasites, and the fever was quartan in type unless several broods of parasites were present.

ii. By subjecting 3 monkeys infected with *P. brasilianum* to a reversal of the normal 12-hour periods of light and dark for from 21 to 43 days, the customary periodicity of the reproductive cycle was altered so that, within 2 to 3 weeks, sporulation occurred at a maximum rate just after 8 p.m., instead of just after 8 a.m. In one of the monkeys, the one brood of parasites present split into two broods, one of which sporulated 12 hours before, and the other 12 hours after, the original brood had sporulated.

iii. Monkeys with a latent infection of *P. brasilianum* proved immune to inoculations with the same strain and also to inoculations with the other strains tested. This immunity was effective immediately after the initial infection had abated and it lasted for at least a year (as long as tested).

W. F.

JERACE (Felice). Osservazioni sui rapporti tra intensità dell'infezione, durata del periodo di incubazione, tipo febbrile e decorso clinico della malaria umana indotta con anofeli o con sangue. [**Intensity of Infection, Incubation Period, Type and Course of Inoculated Malaria.**—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 6. pp. 694-704. With 3 graphs. English summary (9 lines).

The author has studied the results of inoculating 52 general paralytics with malaria, 22 of them by mosquitoes and 30 by injection of blood from a patient with benign tertian parasites. The points for special observation were : (1) *The effect of the number of biting anopheles on the period of incubation.* He found that with up to ten anopheles the average incubation was 15.5 days, with more than eleven 13.7 days. Also with recently infected mosquitoes, up to ten days, the period was 14 days, with those infected earlier, from 11 to 30 days, the period was 16.5 days. The general average worked out as 14.5 days.

(2) *Comparison between mosquito infection and that by direct inoculation of blood* in the effects on incubation period, type of fever and duration of the acute fever, i.e., number of febrile attacks. The incubation

period was on an average 12.5 days after blood inoculation, or two days shorter than that with mosquitoes. As regards the type of fever : after mosquito infection among the 22, fourteen or 63 per cent. had quotidian fever, 6 or 27 per cent. tertian fever and 2 or 9 per cent. a mixed type. In contrast, of the 30 inoculated with blood direct, 14 or 47 per cent. showed quotidian, 12 or 40 per cent. tertian, and 4 or 13 per cent. a mixed type of fever. Thirdly, as regards duration, in 27.3 per cent. (6 cases) only of those infected by mosquitoes did the fever come to an end spontaneously, *i.e.*, without the use of quinine, whereas in 13 of the direct blood infected or 43 per cent. this spontaneous cessation took place.

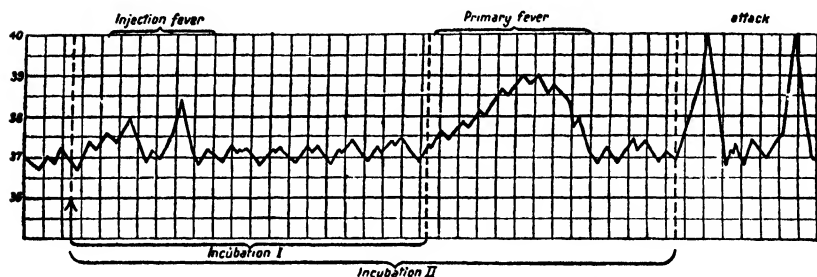
H. H. S.

V. ASSENDELFT (F.). **Therapeutic Malaria. A Parasitologic Study.**—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 6. pp. 679–693. With 11 figs.

The primary fever which is usually tertian in the natural malaria of Holland is more often quotidian in therapeutic malaria.

These observations were made on 350 cases of benign tertian therapeutic malaria ; 288 were infected by means of subcutaneous injection, 32 by intravenous injection, 30 by mosquito bites. A fever which the author calls " injection fever " occurred during the first 3 days in 43 per cent. of the patients inoculated subcutaneously ; he attributes it to the multiplication of the parasites at the site of inoculation. When only a few parasites were inoculated, this fever did not arise ; when the number was over 10 million it occurred in 80 per cent., but when it was less than a million it did not occur at all. The length of the incubation period is influenced by the number of parasites injected, the compatibility of the blood of donor and recipient, relative immunity, etc. A fever occurs in primary infections at the end of the incubation period ; this lasts about a week and is known as the " primary fever " ; it is only slightly remittent. Primary fever does not often occur in patients who have had malaria before. The primary fever is followed by the attack which is of tertian type in the naturally acquired malaria of Holland, but is more often quotidian in therapeutic malaria where inoculations are made from patient to patient. The parasites have a tendency to form a second generation, and consequently two generations are often inoculated. The smallest number of parasites which is sufficient to cause fever, or the " pyrogenic limit," differs in different patients, and may be anything from 2 to 12,000 per cubic millimetre.

W. F.



Normal fever curve in therapeutic malaria, showing injection fever (due to the development of parasites *loco injectionis*), primary fever and attacks.

[Reproduced from the *Rivista di Malariologia*.]

WHITE (R. Senior). **Three Years Mosquito Control Work in Calcutta.**—*Bull. Entom. Res.* 1934. Dec. Vol. 25. Pt. 4. pp. 551-596. With 10 figs. [72 refs.]

The number of kinds of mosquitoes known to occur in Calcutta is 46, and, although very few of these are of importance either economically or numerically, species which are vectors of malaria, filariasis, dengue and yellow fever are abundantly represented. Notes, chiefly concerned with bionomics, on all but two of the forty-six species are given. Those against which, owing to the numbers in which they are present or their importance as disease-carriers, work is required are:—*Anopheles subpictus*, *A. vagus*, *A. stephensi*, *Culex fatigans*, *C. vishnui*, *C. tritaeniorhynchus*, *C. gelidus*, *Aedes aegypti* and *Aë. albopictus*. In addition, constant watch must be kept against the introduction of *Anopheles sundaicus*, "the notorious malaria-carrier of the Netherlands Indies and the Andamans."

The greatest pest in Calcutta is, however, *Culex fatigans*, to the bionomics of which, including a résumé of relevant literature from 1919 to 1934, the major portion of the present paper is devoted. In Garden Reach, in the third year of control, *C. fatigans* still formed "65 per cent. of the total mosquito catch," and two-thirds of the specimens of this species caught annually are secured from January to April, when rainfall is low. Very little is yet known as to the exact breeding requirements of the insect, and investigation of breeding-places by specialists in the chemistry and bacteriology of sewage would probably yield valuable data. Meantime it is of interest to note that the open sewers to the east of Calcutta, stagnant or nearly so except at periods of heavy rain, are "simply enormous elongate breeding-places, where larvae can be spooned up at an almost unbelievable density."

Culex fatigans, of which the adults are on the wing in all stages, from newly emerged, unfed females to those which are ready to oviposit, appears to move about chiefly during the first two hours of darkness. In a controlled area it is possible, from the percentage of Stage I adults found in morning catches, to determine whether the control work is satisfactory.

E. E. Austen.

COVELL (G.). **Note on the Control of Mosquitoes and Malaria in Delhi.**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 273-289. [28 refs.]

The official policy in Delhi for the last 25 years has been to call for repeated reports and then to ignore the advice given.

The mosquito nuisance complained of in Delhi during April is entirely due to the prevalence of culicine mosquitoes, chiefly *Culex fatigans*. It has been suggested that the Kilokri Sewage Farm, situated at some distance from the town, is the source of these mosquitoes, but the author thinks it highly probable that most of the trouble is caused by local breeding in New Delhi itself. Expert advice on the control of mosquitoes and malaria in Delhi has been sought and given on many occasions during the last 25 years. For example Colonel SINTON has visited the city on four occasions, and has submitted three reports; Dr. MACDONALD has made two visits and has also submitted a detailed report. Unfortunately only a small proportion of the permanent measures recommended has been carried out. For example: "Every-one of the many experts who have been called in to investigate malarial

conditions in Delhi has laid down that borrow-pits should be filled or drained, and that in future all excavations of this nature should be strictly prohibited. Yet during the last 3 years, fresh borrow-pits have been created as follows : . . . It is difficult to refrain from the comment that a community which allows this state of things after so many warnings deserves all the malaria and mosquito nuisance that it gets. . . . It is not considered that the control of mosquitoes and malaria in Delhi will ever be really satisfactory until a whole-time fully-trained malaria officer is appointed." The author understands, however, that the prospect of such an appointment being made is exceedingly remote. W. F.

WILLIAMSON (K. B.). The Control of Rural Malaria.—Reprinted from *M.A.H.A. Magazine* [Malayan Agri-Horticultural Association]. 1933. July & Oct. Vol. 3. Nos. 3 & 4. pp. 145–150 ; 201–206 ; 1934. Jan. & Apr. Vol. 4. Nos. 1 & 2. pp. 224–228 ; 281–291.

The author advocates the use of rotting vegetation (Herbage Cover), metallic poisons, and sluicing to control mosquito breeding.

"The principles directing the control of malaria must accommodate themselves to two facts : firstly that the cost of effecting it by current urban procedures would be prohibitive, and secondly, that rural areas, with few exceptions, lie outside the possible range of skilled medical control." Some waters are rendered unsuitable by nature for the breeding of anopheline larvae, and the author's thesis is that these natural methods should be imitated and developed in order to free rural areas from malaria. The costs of ordinary subsoil drainage are prohibitive in such districts, except when money from general revenues is poured into small rural areas, as has been the case in Singapore and Penang. The waters of the coastal flat land of British Malaya are unsuitable for the breeding of the dangerous carrier *A. maculatus*. One of the main reasons for this is the presence of rotting vegetation, and this can be imitated by adding vegetable matter to the water of breeding places. "We can also regulate and multiply the sluicing effect seen in rapid streams after storms. Its effectiveness is probably the result of several things besides larvae being washed away." The larvae and eggs are stranded high and dry, the composition of the water is probably changed by the disturbance of the bed of the channel, and breeding ceases to occur. Oiling is unsuited for rural areas, not only because it is too expensive, but also because it kills crops and fish. Paris green, in Malaya, has been found dearer and less suitable than oil. There is no danger of arsenical poisoning from Paris green because a fungus, a *Penicillium*, causes it to be dissipated in the form of arseniuretted hydrogen, which does no harm in the open air though it has led to poisoning in rooms papered with wall-papers containing arsenical pigments. The possible effects of light and sound rays upon mosquitoes are discussed, but the author does not consider them likely to be of much practical value.

He has investigated the effect of slowly-dissolving mineral poisons upon larvae, and has found that the larvae of *A. maculatus* die within 5 days when copper or brass is present in the water. "The practical problem is to procure cheap ores or residues, slightly more soluble than most of the compounds tested in the laboratory, which will ensure that the minute traces of copper needed to safeguard breeding waters will be maintained in spite of rain and seepage flow ; and a search for these

is being made. Slow mineralization promises a possibility of effective control which may reduce the labour cost of treating pools and seepages to a fraction of what it now is. . . . But the method is clearly inapplicable to rapidly running water, and its usefulness in ponds and marshes is doubtful. On the other hand, the coppering of containers in towns threatened with yellow fever might be an invaluable aid in fighting the disease if it ever appears in this country." Another natural method is specially mentioned, it is known as "Herbage Cover."

"Shallow water up to a few inches deep is covered with plucked grass and herbage, or the leaves of trees . . . with a few twigs intermixed so as to form a brushwood drain for running water. The herbage is well trampled under foot until it forms an almost solid wall a foot or more in height . . . it cannot be penetrated by egg-laying mosquitoes; it provides dense shade and, at least in stagnant water, sufficiently concentrated rotting to prevent the breeding of malarial species . . . very little dislocation of the herbage occurs in ordinary hillfoot or other drains, if their lower ends are provided with a double row of stakes to keep the solid mass of vegetation in position. . . . The method is particularly effective for stagnant pools where the biochemical effects of the rotting vegetation are greatest. . . . It is therefore probable that by this simplest, speediest, and cheapest of all anti-malarial measures, much of the malaria of the hills and hill valleys might be stamped out, if measures were taken to teach it to villagers. . . . To limit effort to oiling, which is better suited for dealing with the malaria . . . in other countries, is to disregard the help to be derived from local circumstances, and to fly in the face of reason and common sense. . . . Fish ponds should everywhere be established at the heads and along the course of the dangerous irrigation channels in hill rice valleys; and should be used to sluice the channels."

[Sluicing has not proved satisfactory in other parts of the Malay States. *Ante*, p. 139.] W. F.

MORIN (Henry G. S.). Note préliminaire sur un dispositif économique pour la destruction des larves d'anophèles dans certains ruisseaux. [An Economical Method for the Destruction of Anopheline Larvae in Certain Streams.]-*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Oct. Vol. 12. No. 8. pp. 743-746. With 3 figs.

The principal vectors of malaria in the highlands of Indo-China are stream-breeders, and when the rains come they are washed away by the flood. The author seeks to imitate this by artificial flushing. He has seen streams in Penang and in the Malay States which are treated with success in this way, thus saving the cost of oiling, etc. A barrage is built across the stream, and twice a week the impounded water is released by a coolie, and the stream is washed out. Diagrams are given of a siphonage apparatus designed by the author which would do this automatically.

[The difficulty in Malaya has been that the whole erection is washed away in the heavy rains. *Ante*, p. 139.] W. F.

STRUTHERS (E. A.) & SINHA (S. N.). The Use of Bamboo in Subsoil Drainage. Review of Three Years' Experiment.-*Malayan Med. Jl.* 1934. Dec. Vol. 9. No. 4. pp. 197-199.

Bamboo pipes have been used for subsoil drainage in the Malayan town of Kuala Lipis for the last 3 years, and the authors conclude that this method is of use in isolated places where the cost of transport of oil or tile pipes is high, and where bamboos are plentiful.

The pipes are prepared by sawing through the stems on either side of the nodes and as close to the node as possible. They should have a diameter of not less than 3 ins. They are prepared by soaking in water in order to get rid of the internal pith coating. They are buried at least 5 ft. deep. The upper surface of the joints between the pipes is luted with clay in order to prevent the entrance of silt. Inspection pits made of tile pipes set vertically are put in at all junctions; the bamboo at the bottom of the pit is cut in half to form an open invert. [See this *Bulletin*, Vol. 31, p. 153.] W. F.

DE BENEDETTI (Augusto). Considerazioni tecnicopratiche sui metodi di lotta contro le larve anofeline. [**Measures against Anopheline Larvae.**]*—Riv. di Malariologia.* Sez. I. 1934. Vol. 13. No. 3. pp. 365–371. [10 refs.] English summary (5 lines).

The author discusses a method for causing Paris green to float for a long time.

In an earlier communication (this *Bulletin*, Vol. 31, p. 710, and *Riv. di Malariologia*, Vol. 12, pp. 92–97) the author described a method of mixing small quantities of mineral oil with ordinary garden soil, which was then heated and used as a diluent for Paris green. He now gives further details of his method of application and describes several experiments. In one, which was carried out in a bucket and not under field conditions, arsenic was discoverable chemically after 27 days, and though the quantity was very small, larvae were killed on that day within 24 hours.

[It seems that we have here an original idea, and it should surely be possible to discover more precisely how to render the soil and Paris green unsinkable and whether the Gutzeit test for arsenic is appropriate. It appears desirable that experiments should be carried out on several types of water in the field.] P. A. Buxton.

WASSILIEFF (A.). Expériences sur un nouveau produit arsenical larvicide. [**A New Arsenical Larvicide.**]*—Arch. Inst. Pasteur de Tunis.* 1934. Dec. Vol. 23. No. 4. pp. 449–454.

The copper arsenite prepared by the author is far cheaper than Paris green and equally efficient.

The drawbacks to Paris Green are its high price and the complicated machinery required for its manufacture. In order to be effective it must contain at least 50 per cent. of As_2O_3 , and this makes it expensive. A preparation of arsenite of copper, known as "Arsmal," has been made in Russia (this *Bulletin*, Vol. 31, p. 57), it contains only 8.86 per cent. of As_2O_3 , costs only a fifth of the price of Paris green, but is equally efficient as a larvicide. The author describes the method by which he has made copper arsenite from As_2O_3 , $CuSO_4$ and $CaCO_3$. The results confirmed the work done in Russia. It was as effective as Paris green in destroying larvae under laboratory conditions, it was easy to prepare, and far less costly. The powder is finer than Paris green. W. F.

TREILLARD (M.). Destruction saisonnière domestique des anophèles adultes (*H. minima*) pour la prophylaxie antipaludique en Indochine méridionale. [**The Destruction of Adult Anopheles as an Anti-Malaria Measure in S. Indo-China.**]*—Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 937–939.

The author recommends an apparatus, similar to that employed in smoking out bees, for destroying anopheles in the coolies' huts on the

rubber-estates of South Indo-China. The fumigant is cresyl which drips slowly, from a reservoir, on to a hot-plate. The vapour is directed by bellows into all corners and crannies. This method is specially suited to *A. minimus* for it remains in habitations after feeding. It should be applied for several weeks before and after the rains. W. F.

RUSSELL (Paul F.). **Zooprophylaxis Failure. An Experiment in the Philippines.**—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 5. pp. 610-616.

Zooprophylaxis is not only of doubtful value in the Philippines, but may actually be a danger. It has nowhere been shown to be an effective direct weapon against malaria. On alternate nights, the author tied up four buffaloes, one on each side of a native house at a distance of a few yards. Inside the house was a man under a mosquito net. The mosquitoes in the house were caught every 2 hours during the night for a period of two months. Many more anophelines were caught when the buffaloes were present than when they were absent. When an animal barrier was present, three times more anopheles were caught than on the nights when there was no barrier. W. F.

WILLIAMS (Louis L.), Jr. **Civil Works Administration Emergency Relief Administration Malaria Control Program in the South.**—*Amer. J. Pub. Health*. 1935. Jan. Vol. 25. No. 1. pp. 11-14.

Antimalaria drains have been dug by the Unemployed under the Relief Works Scheme.

The Federal Emergency Relief Administration was organized in the spring of 1933, and relief labour has been utilized for the control of malaria. The Public Health Service supplied the technical supervision for the drainage work and was given \$350,000 by the Civil Works Administration. Nearly 6,000 miles of drains were cut which drained 100,000 acres of pond and more than 200,000 acres of swamp. The trend of malaria in the United States has been steadily downwards for the last 70 years, with a few slight interruptions; one of these occurred in the summer of 1934, when there was more malaria than at any time during the last 20 years. It is encouraging to note that this increase in malaria has not affected those districts where Emergency Relief projects have been completed. W. F.

MOSNA (Ezio). La chinoplasmina usata nella profilassi della malaria. [**Quinoplasmine in Malaria Prophylaxis.**]—Reprinted from *Riv. "Croce Rossa"*. Rome. 1934. Vol. 9. No. 6. 15 pp. With 5 graphs.

Administration twice weekly of quinoplasmine (2 cgm. to adults with doses proportionately less for children) to the entire population of 771 in a commune where malaria is hyperendemic, during a period of five months (18th May-21st October) has resulted in (1) a marked reduction in malaria incidence among the population in general; (2) marked reduction in incidence among those born during the year; (3) absence of infected anopheles throughout the period of experiment; (4) absence of symptoms of toxicity or intolerance of the drug.

In 1931 MISSIROLI and MARINO treated the whole population of Torpè (East Sardinia) for a period of 10 days in April and June with quino-plasmine and adduced therefrom that the prophylaxis so obtained is of brief duration and that continued treatment of all patients with fever does not eliminate all sources of infection because many when first seen have gametocytes in their blood [see this *Bulletin*, Vol. 31, p. 473].

In the following year they treated the whole population on alternate days in June and July, the time of greatest prevalence of anopheles. As a consequence they found no infected anopheles during this period and that the time of maximum incidence of malaria was postponed to September. MISSIROLI and MARINO deduced that it would be possible to control, if not eradicate, malaria in hyperendemic zones by administration of this drug on alternate days throughout the time of malaria transmission. During the two months preceding the experiment described in this article examination of 191 children under 12 years living in Posada, on the east coast of Sardinia, 6 kilometres from Torpè, revealed a splenic index of 96 per cent. and a parasitic index of 48 per cent. The experiment consisted in administering quinoplasmine (quinine 0.3 gm. with plasmoquine 1 cgm.) twice weekly in doses of 2 cgm. to adults and correspondingly reduced doses to children, 0.25 cgm. to those under one year, 0.5 from 1-6 years, 1.0 from 6-12 years, 1.5 from 12-19 years. Administration was continued from 18th May to 21st October to 725 out of an entire population of 771. They were, for convenience, divided into three groups for treatment on different days. The only signs of intolerance were gastralgia (2 cases), giddiness and asthenia (6 cases). During the period careful search was made for all cases of malaria and any found was promptly treated with quinine for 10 days in conjunction with plasmoquine twice a week.

Special points studied were: (1) the number of cases of malaria among the population; (2) the number among children born during the year; (3) the infection of anopheles; (4) the splenic and parasitic indices.

As regards the first, the inhabitants of the neighbouring Torpè, where quininization only was used, served as a control. The greatest number of cases occurred in August in both places, but whereas in Posada there were only 22 cases per 1,000 inhabitants, in Torpè there were 126, and during the whole period of observation there were 95 in the former and 276 in the latter, per thousand. The effect on gametocyte carriers is also worth noting. At Posada only two were found, one each with *P. vivax* and *P. falciparum*; at Torpè there were 44 with *P. vivax* gametocytes and 30 with those of *P. falciparum*.

The second point, the number of children born within the year attacked with malaria. In 1930 there were 14 attacked out of 49 or 48 per cent.; in 1931 and 1932 seven out of 30, or 23 per cent.; in the experimental period, 1933, only three out of 31 or under 10 per cent.

Thirdly, infection of anopheles. Of 816 caught in Posada in June-September not one was found infected, whereas among 572 caught in Torpè there were 10 or practically 2 per cent.

Fourthly, the splenic index in the successive years 1931-34, taken in March, has been 12.5, 5, 8.9 and 0.5 per cent. (in January 1930 it was 26.3), taking count of spleens enlarged to the umbilicus level; the percentages of non-palpable spleens have been 3, 6, 3.7 and 29.5 in the corresponding years. The parasitic indices from 1930-34 have been 42.2, 30, 32, 48 and 20 per cent. respectively.

H. H. S.

PIKUL (J.), SERGUIEV (P.) & TIBOURSKAYA (N.). [**Experiment on the Prophylactic Use of Plasmocide in Daghestan with Observations on the Mosquito Infection Rate.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 4. [In Russian pp. 322–329. With 6 figs. [11 refs.]]

The greater part of this paper is devoted to an account of the result of treatment of the population of a restricted area with plasmocide. This was found to have a satisfactory schizontocidal and a marked gametocidal action in BT and MT (in the latter case it was combined with quinine). There was a diminution of the infection-rate in mosquitoes captured in the same area after mass treatment has been carried out. Prophylactic treatment with plasmocide is only briefly referred to: a group of 64 persons was treated with doses of 0.03 gm. administered two days in succession—followed by an interval of three days—but no protection resulted, since in 14 cases primary infections occurred during the period of treatment. C. A. Hoare.

KOMP (W. H. W.) & CLARK (H. C.). **A Third Year's Observation in Panama, with Special Reference to Control with Atabrine.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 381–406. With 1 fig.

An adverse report on atabrin in the control of malaria. The danger of an oasis of malaria control in a region of high endemicity.

In August 1932, 24 cases of malaria among native Panamanians living along the Chagres River were treated with three $1\frac{1}{2}$ grain tablets of atabrin daily for 5 days. Their bloods were examined monthly for 8 months, and, by the end of this period of observation, 19 of them had relapsed. In January 1933, a number of towns along the same river were surveyed, and the positive cases were treated with atabrin administered personally by the senior author. Each month, for a period of 8 months, these towns were revisited, and again those found positive were given a five-day course of atabrin. There were many relapses; indeed the results in the atabrin treated towns were very little better than in a town where quinine was distributed by a native woman, and, as 5 days atabrin treatment costs about $2\frac{1}{2}$ times as much as 5 days treatment with quinine, the authors conclude that "the use of atabrine does not seem to be a practicable method of malaria control under the conditions existing in certain native villages in Panama." Atabrin did not affect the power of crescents to infect mosquitoes; abundant infection occurred in *A. albimanus* as the result of feeding upon atabrin-treated patients whose blood contained only crescents. As usual in work of this sort it was found impossible to treat all those found positive in the monthly surveys, because of their absence during the succeeding treatment period.

Though nearly every inhabitant of these river towns is infected with parasites, there is very little clinical malaria, and, during the past three years, the authors have not heard of a single death from malaria. "This of itself bespeaks a high tolerance for the disease." Certain persons were met with whose blood remained free from parasites for a year or more, and who then were attacked by clinically severe malaria. "It seems that the severity of clinical symptoms is greater in these 'primary' cases which occur after a long period of freedom than it is in cases which increase to clinical proportions from time to time in the course of a more or less continuous latent infection. This and similar

observations by other workers would lead us to believe that there is a certain element of danger in successful control of malaria to the inhabitants of any circumscribed area lying within a region of high endemicity. If continued freedom from parasites means a gradual loss of tolerance, the inhabitants of such an oasis may suffer severely from epidemics of malaria originating from introduced cases, so that their last state would be worse than their first." W. F.

RUSSELL (Paul F.). **Avian Malaria Studies, IX. Atabrine as a Prophylactic Drug in Sporozoite Infections of Avian Malaria.**—*Philippine Jl. Sci.* 1934. Aug. Vol. 54. No. 4. pp. 483–493. [17 refs.]

Canaries were given intramuscular injections of atabrin for a few days, and were then inoculated with the sporozoites of *Plasmodium capistrani* from infected *Culex fatigans*. The atabrin did not act as a prophylactic against the sporozoites. It neither prevented infection nor lengthened the period of incubation. W. F.

MEHTA (Dev Raj). **Studies on the Longevity of Some Indian Anophelines. Part I. Survival of *Anopheles subpictus* Grassl under Controlled Conditions of Temperature and Humidity.**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 261–272. With 2 charts & 1 fig. [33 refs.]

A. rossii (*subpictus*) does not live long enough to act as a carrier in nature.

It has been suggested that the reason why *A. rossii* (*A. subpictus*) though easily infected in the laboratory is not a carrier in nature may be that it does not live long enough in the hot weather of the malaria season to allow the development of the parasites. These experiments were conducted at the Ross Field Experimental Station for Malaria at Karnal in order to test this hypothesis. The technique employed is described and illustrated. It was found that at 95°F., with humidity ranging from 30 to 90 per cent., *A. subpictus* lived from 3 to 8 days, and at 86°F. it lived from 6 to 14 days. "It is concluded that the females of *A. subpictus* live, for the most part, from 5 to 11 days at 30°C. (86°F.), and therefore the sporogonous cycle of the malarial parasite cannot be completed during the life of the mosquito host. This is one of the important factors elucidated to explain why *Anopheles rossii* (*subpictus*) is not a 'carrier' of malaria in nature."

W. F.

BOSE (K.). **Larval Survey of the Land around Birnagar and Determination of the Longevity of the Local *Anopheles culicifacies* and its Habits.**—*Records of the Malaria Survey of India.* 1934. Sept. Vol. 4. No. 3. pp. 253–259. With 1 map.

A. culicifacies occurs here, but it is harmless. *A. philippinensis* is the carrier.

This survey was made under the auspices of the Birnagar Palli Mandali (Bengal). The results point to *A. philippinensis* as the principal carrier in the surrounding villages, as it is in Birnagar itself. The country round the town consists of rice-fields interspersed with villages. No *A. philippinensis* can be found in the rice-fields; here the

commonest species is *A. hyrcanus* var. *nigerrimus*. The chief breeding places of *A. philippinensis* are the ponds and lakes, known as bails and tanks, which are overgrown with weeds. *A. culicifacies*, the notorious carrier of the Punjab and Southern India, breeds during the dry weather in the Churni River which flows past Birnagar; but during the rains and the fever season it becomes scarce. No infected specimens have been found in the district, and it appears to be unimportant.

W. F.

TOUMANOFF (C.). Observations sur les habitudes trophiques des anophélines de la colonie de Hong-Kong. [**The Trophic Habits of the Anopheles of Hong Kong Colony.**—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 745-749. With 3 figs. on 2 plates.

A study of zoophily in the Far East.

In Shing-Mun, a temporary labour settlement, and Wo-Li-Hop, a small village, both situate in the colony of Hong Kong and with the same anopheline fauna, the percentage of naturally infected mosquitoes is very different. According to JACKSON, dissection of 2,155 *Anopheles minimus*, 10,936 *A. jeyporiensis*, 230 *A. maculatus*, and 2,818 *A. hyrcanus*, caught at Shing-Mun, showed 12.48, 9.93, 3.48 and 1.21 as the respective percentages of infection; at Wo-Li-Hop, among 1,185 *A. minimus*, 3,707 *A. jeyporiensis*, 187 *A. maculatus*, and 176 *A. hyrcanus*, the corresponding percentages were 3.63 and 3.21 for the first two species, while dissection of the others was negative. The explanation of this striking discrepancy would seem to be "animal deviation." At Wo-Li-Hop, where there are many buffaloes, oxen and pigs, the cowhouse, though sometimes separate, is often divided from the dwelling merely by a wall, while the pigsties are usually solidly built and well shut in. Animals at Shing-Mun, on the other hand, apart from dogs and goats, are practically non-existent. By way of control, precipitin tests (results given in a table) were made of the stomach-contents of mosquitoes caught at the two villages mentioned, and of others taken at Shouson-Hill in Hong Kong Island, where livestock consists chiefly of pigs kept in sties of a type unlikely to shelter anophelines. At Shing-Mun, where there are no cattle or pigs, 89 per cent. of mosquitoes of the four species mentioned above were gorged with human blood; at Wo-Li-Hop, on the other hand, out of 92 *Anopheles* caught for the most part in cowhouses, only 7 contained human blood, and even 23 out of 26 specimens of the notorious *A. minimus* proved to have been feeding on buffaloes.

In the opinion of the author, these and other results of what is admittedly a preliminary investigation "demonstrate the interest of the study of zoophily and of prophylaxis by means of zoophily in the Far East, and the possible importance of the correct housing of livestock as affecting the incidence of local endemic malaria."

E. E. A.

TOUMANOFF (C.). Quelques faits sur les habitudes trophiques des anophélines d'Extrême-Orient. [**Notes on the Trophic Habits of the Anophelines of the Far East.**—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 932-936.

As is shown in a table, all oriental anophelines may attack animals, and precipitin results hitherto obtained serve to stress the importance

of the study of zoophily in the Far East. In the case of *Anopheles minimus* and *A. jeyporiensis*, chief malarial vectors in Indo-China and Hong Kong, buffaloes rather than cattle seem, on occasion, to replace man as hosts, and may perform a similar office for other paucidentate species. On the other hand, multidentate species, adapted to feeding upon livestock and of little or no account as malaria-carriers, have been found gorged with bovine blood where cattle alone were present. Where cattle but no buffaloes are kept *A. minimus* is definitely androphile, whereas *A. vagus*, governed perhaps, as are also probably other zoophile species, by an imperious tropism, batters especially on ox-blood.

The proportion of female mosquitoes of innocuous, non-malaria-carrying species found gorged with human blood inside dwellings is relatively small: thus, out of a total of 334 precipitin tests of the stomach contents of *A. hyrcanus* var. *sinensis*, *A. tessellatus*, *A. subpictus*, *A. barbirostris* and *A. vagus*, only 20 (5.9 per cent.) showed human blood. In the case of *A. vagus*, out of 261 tests on specimens caught in dwellings, only 9 reactions were positive with anti-human serum, and the percentage of animal blood in this species is sometimes 100.

In Cochin-China, contrary to what happens in Europe in the case of *A. maculipennis*, the absence of perfect stalling for cattle does not hinder completely the deviating effect of livestock upon the innocuous anophelines, which frequently use dwellings merely as retreats after feeding. Thus there is often an absence of correlation between the trophic habits of anophelines in Cochin-China and their ascertained presence in habitations. It is especially where livestock is absent or scarce that the innocuous *Anopheles* in houses contain human blood; in such places, should they have access to gamete-carriers, they may become dangerous.

A postscript by ROUBAUD emphasizes the theoretical and practical interest of Toumanoff's observations on deviation by the buffalo of paucidentate, typically androphile anophelines in the Far East.

E. E. A.

TOUMANOFF (C.) & HU (S.). Premières données sur la zoophilie de *A. hyrcanus* var. *sinensis* en Chine (région de Shanghai). [**Zoophily of *Anopheles hyrcanus* var. *sinensis* in the Shanghai Region.**—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 741-745.]

Although several times found infected in nature (on one occasion in Sumatra 12 per cent. out of 3,638 specimens dissected were positive), *A. hyrcanus* var. *sinensis* as a vector of malaria is considered to be practically negligible. This mosquito, which has a well developed maxillary armature, feeds freely on animal blood, and as a rule becomes naturally infected only in isolated cases. At the same time, in certain parts of China, especially the regions of Shanghai and Nanking, no other anopheline is known to occur, so that *A. hyrcanus* var. *sinensis* is the only possible carrier of the local malaria. Using the precipitin test on material obtained from a small village some 10 miles from Shanghai, where the mosquito in question is very abundant in summer, both in dwellings and in cattle-sheds, while the incidence of malaria in the district is relatively slight, 295 out of 300 reactions were positive

for buffalo blood, while 4 more showed mixed buffalo and human blood. Thirty-five additional specimens were uniformly positive for buffalo blood. Since *A. hyrcanus* var. *sinensis* can readily be infected experimentally, the importance of zoophily as a safeguard to human communities in China is obvious. In Hong Kong, where cattle are nearly absent, the same species of mosquito is almost invariably gorged with human blood. E. E. A.

TOUMANOFF (C.). Caractéristique des représentants du "Rossii-Ludlowi" groupe de l'Indochine. Première note: *A. subpictus* Grassi. [**Characters of the Indo-Chinese Representatives of the "Rossii-Ludlowi Group."** I. *Anopheles subpictus*.]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Aug.-Sept. Vol. 12. No. 7. pp. 657-673. With 10 figs.

Much of this paper is concerned with a detailed comparison, in both the larval and the adult stages, of the Tongkingese form of *A. subpictus* (syn. *A. rossii*) with *A. subpictus* var. *indefinitus*, as found by KING in the Philippine Is. (see this *Bulletin*, Vol. 29, p. 479), and with the typical form as described by GRASSI. Notes are also given on the diagnostic characters of *A. subpictus* as it exists in Cochin-China, and on those of *A. vagus* in Tongking. Though in both Southern and Northern Indo-China *A. subpictus* appears to belong to the var. *indefinitus*, in Cochin-China it is to some extent intermediate between the variety and the typical form. *A. subpictus* in Tongking is best distinguished from *A. vagus* by the amount of black on the palpi in the female, and in the male by the length of the filament of the phallosome.

To what extent, if any, *A. subpictus* is a malaria-carrier, whether in Tongking or in Cochin-China, it is as yet difficult to say. E. E. A.

TREILLARD (M.). Tableau synoptique pour la détermination rapide des anophèles d'Indochine. I. Adultes. [**A Synoptic Table for the Rapid Determination of the *Anopheles* of Indo-China. I. Adults.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 751-753.

Although numerous keys for the determination of Far Eastern *Anopheles* already exist, it is claimed by the author that the dichotomic method is not without drawbacks, chief among which are final uncertainty and the impossibility of comparing the same characters in all species, and the different species one with another. Figures of whole insects, in black-and-white or in colour, are likewise open to objection, and are difficult to manipulate. Taught by experience, Treillard prefers a combination of synoptic table and diagram, by means of which reliable determinations may be arrived at with ease and rapidity. The table at the end of this short paper includes, besides other details, a schematic representation of leg- and palp-markings in twenty-one species of *Anopheles* found in Indo-China. E. E. A.

EVANS (A. M.). **Further Notes on African Anophelines, with a Description of a New Group of *Myzomyia*.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 549-570. With 11 figs. [13 refs.]

In this paper, which is purely systematic, notes are given on *Anopheles distinctus* and its allies, and the following new species and

varieties are described :—*A. distinctus* var. *ugandae*; *A. Myzomyia schweizeri* (Belgian Congo; French Sudan); *A. theileri* var. *septentrionalis* (Uganda; Anglo-Egyptian Sudan); *A. (Myzomyia) wilsoni* (Tanganyika Territory); and *A. (Myzomyia) lovettae* (Tanganyika Territory). The two latter species constitute the new group *Eomyzomyia*, which is likewise described. The author also furnishes a "Provisional Key for separation of the females of *A. distinctus* and the Anophelines resembling it"; discusses the systematic position of *A. rufipes*; and adds notes on certain morphological characters of *A. ardensis*, *A. machardyi*, and *A. natalensis* and its var. *multicinctus*.

E. E. A.

BUXTON (P. A.). Further Studies upon Chemical Factors affecting the Breeding of *Anopheles* in Trinidad.—*Bull. Entom. Res.* 1934. Dec. Vol. 25. Pt. 4. pp. 491–494.

BEATTIE, working in Trinidad, found, with regard to the hydrogen-ion concentration and CO₂ content, that "no definite correlation exists between the reaction of the water and the prevalence of *A. tarsimaculatus*" (see this *Bulletin*, Vol. 30, pp. 293–294). Nevertheless the prevalence of larvae of this mosquito in ponds appeared to vary inversely with the amount of ammonia nitrogen in the water, and there was reason to think that oviposition was possibly affected by this factor.

In the present paper Buxton endeavours "to make fuller use" of BEATTIE's original and hitherto only partly published data. As regards ammonia nitrogen, it is shown in a table that, although there is no very close correlation, "as the concentration of ammonia nitrogen rises, the number of larvae falls." When the numbers are examined statistically, it appears that "the effect of ammonia nitrogen only accounts for a little more than 12 per cent. of the variation in the number of larvae." In rice-field waters alone correlation is higher, but "only a little more than 18 per cent. of the variation in the number of larvae is attributable to the ammonia nitrogen." Since the figures of the latter are not uniformly high in all rice fields, it is probable that the ammonia results from sewage contamination rather than the actual cultivation of rice.

A second table, dealing with organic nitrogen, and the number of occasions when *A. tarsimaculatus* larvae were found in its presence, shows it to be a factor of less importance than that of ammonia nitrogen. While the conclusion that the latter "has a greater effect upon the numbers of larvae in Trinidad than any other of the factors which were studied" is possibly sound, the determination of the manner in which this factor acts is a matter for laboratory experiment rather than work in the field.

E. E. A.

HILL (Rolla B.). Feeding Habits of Some Venezuelan *Anopheles*.—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 425–429.

Nine hundred *Anopheles* of various species, caught between July and October 1929, in three localities in the Lake Valencia region of Venezuela, where malaria is serious, were subjected to the precipitin test in order to determine the source of ingested blood. The results indicate that *A. albimanus* "feeds on human beings in large numbers,

and is probably the most dangerous species usually found in the Lake Valencia region" (out of 506 *A. albimanus* tested against human serum, 170, or 34 per cent., proved positive). *A. bachmanni*, although like *A. tarsimaculatus* definitely preferring animal blood, was positive to human antiserum in 14 cases out of 262 individuals tested, and is therefore "confirmed as a possible malaria carrier." *A. pseudopunctipennis*, on the other hand, though of importance in Argentina, would seem to be but a doubtful vector in the area mentioned above. *E. E. A.*

RUSSELL (Paul F.) & SANTIAGO (Domingo). **Flight Range of Anopheles in the Philippines. Second Experiment with Stained Mosquitoes.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 407-424. With 4 figs. & 1 map.

In continuation of a previous experiment by the authors on similar lines (this *Bulletin*, Vol. 31, p. 720), 10,000 stained mosquitoes, chiefly of the *Anopheles funestus-minimus* subgroup, were released from one point. Out of 31,011 adult anophelines afterwards collected in all directions therefrom, up to a distance of 4 kilometres (2½ miles), 11 were stained. All but two of these were retaken to the south of the liberating place, during a strong north-east monsoon, and they included 8 examples of *A. minimus* var. *flavirostris*, "the chief malaria carrier of the Philippines," an engorged female of which was recaptured between 1½ mile and 1 mile 660 yards down wind. It is concluded that *A. minimus* var. *flavirostris* (as also *A. subpictus* var. *indefinitus*) flies with, rather than against the wind, and in this way may travel at least 1½ mile; also that "the northeast monsoon may have a pronounced effect in extending the flight range of the malaria-carrying anophelines of the Philippines." *E. E. A.*

PIRES (Rubens Escobar). Contribuição para o estudo dos Anophelinos do grupo Nyssorhynchus (Diptera, Culicidae) do Estado de São Paulo. [A Study of the Anophelines (Nyssorhynchus Group) in the State of São Paulo.] [Thesis for Doctorate, Medical Faculty, São Paulo.]—89 pp. 1934. São Paulo: Imprensa Metodista. With 5 charts & 25 figs. [76 refs.]

This thesis, as its title indicates, gives a detailed description of the Nyssorhynchus group of Anophelines as found in São Paulo. The author has also provided keys to facilitate their determination and a series of 25 figures, 20 of them excellent reproductions of microphotographs, depicting special points in morphology. There is also appended an extensive bibliography. The work must have entailed much research and the result will be of service to entomologists and systematists. *H. H. S.*

SHANNON (R. C.). **Malaria Studies in Greece. The Reaction of Anopheline Mosquitoes to Certain Microclimatic Factors.**—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 67-81. With 1 fig.

The importance of the races of *A. maculipennis* in relation to malaria is different. Are these differences inherent, or have the races peculiar ecological needs which tend to cause some of them to seek shelter in houses more than others?

The author endeavours to study the reactions of certain Anopheles to microclimates by making observations in the Struma Valley in Macedonia. His method was to count the females by day in their resting-places, and most of his observations were made in a stable and in certain tunnels and shafts which were excavated for the purpose. With the aid of movable partitions he was able to some extent to control the climatic gradients in the tunnels.

The conclusion is reached that light is extremely important and that probably the light at or about dawn is an effective factor. But when light in a given part of the tunnel is constant, the number of females resting is affected by temperature, there being a preference for lower temperatures within the limits observed. A definite difference between species was noticed, the female *superpictus* tolerating a higher temperature than the female *maculipennis*.

The work is interesting and original, and represents an attempt to carry laboratory observations into the field. As there are so many variables only slightly controllable, it is obvious that the conclusions must be examined very critically. The reader will observe that the author groups together certain days and positions in which the microclimatic conditions appear to be similar, but we cannot discover how consistently the Anopheles behaved on separate days in each group. It would be interesting to see at least one set of figures put out at length and tested for homogeneity; indeed, one might say that, inasmuch as the problem consists of unravelling several factors without the use of strict experimental control, it is essentially statistical. No information is given as to the methods by which temperature and humidity were measured. It would surely be of value to install recording instruments, or at least to measure maximum and minimum temperature. We also lack information about the photometry, a difficult but important subject.

P. A. Buxton.

- i. COVELL (G.). **Anti-Mosquito Measures with Special Reference to India.**—*Health Bull. No. 11. Malaria Bureau No. 3.* pp. ii+61. 3rd Edition. 1934. Delhi. Manager of Publications. [As.12 or 1s. 3d.]
- ii. SINTON (J. A.). **Instructions for Collecting and Forwarding Mosquitoes.**—*Health Bull. No. 13. Malaria Bureau No. 5.* pp. iii+ii+70. With 23 figs. on 2 plates. Revised and Enlarged. Second Edition. 1934. Delhi: Manager of Publications. [As.12 or 1s. 3d.]

i. Although, as indicated in the title, Indian conditions have been specially considered, this extremely useful and valuable pamphlet is really an epitome of the experience gained by many workers in various parts of the world. Originally published in 1927, the booklet in its present edition has been to a considerable extent re-written, and several alterations of practical value have been made. The subject-matter is divided into three parts, respectively entitled:—"Protection against Bites of Mosquitoes"; "Measures directed against Adult Mosquitoes"; and "Measures directed against Larvae of Mosquitoes." It is scarcely necessary to say that, under the latter heading, the various methods of using Paris green, among other chemical larvicides, as a substitute for oil, receive appropriate attention. As regards the amount of oil to be used—a practical question often asked—it is considered that, although to some extent dependent upon circumstances, usually "half an ounce

of oil per square yard, or 15 gallons per acre, is an ample estimate." The advantage of adding a small percentage of vegetable (preferably castor) oil or cresol to increase spreading is duly noted.

A series of short appendices and a concise index conclude a work which should be in the hands of every sanitarian in the tropics.

ii. It is stated in the Preface to this new edition that it is "mainly a compilation of those methods which have been found by the workers of the Central Malaria Bureau and the Malaria Survey of India to be most suitable for the local conditions of this sub-continent." Since, as is now generally recognized, accurate determination of species, which presupposes antecedent good work on the part of the collector, is a primary necessity in any well-planned anti-mosquito campaign, the present treatise, which might be described as "The Intelligent Layman's Guide to Mosquito Collecting," is not the least important among the valuable Bulletins originally issued by the Central Malaria Bureau.

As in the case of the previous number, the precepts enjoined may be studied and followed with profit in any part of the world. *L. E. A.*

MATTHES (H. C.). **A Study of the Seasonal Distribution of Anopheles in Houston, Texas.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 233-248. With 2 graphs.

Apart from brief notes on *A. crucians*, *A. punctipennis* and *A. pseudopunctipennis*, which occur chiefly during the colder months, this paper is concerned solely with *A. quadrimaculatus*, the common and important anopheline in Houston. In the southern section of the city the principal breeding-place is a spring-fed stream or bayou, but rice-fields 15 miles distant also produce adults in enormous numbers. Near the bayou, rainy periods, which cause the water to rise above the aquatic vegetation and thus expose the larvae to the attacks of top-minnows, produce most fluctuations in the abundance of *A. quadrimaculatus*, but the rice-fields area is not affected in the same way. On the other hand winter breeding, though suspended during cold spells, continues when the thermometer rises, and there is no indication that a definite number of broods is produced during the year. A fall of temperature below 20°C. causes rapid decrease in the number of adults, but, in the presence of appropriate breeding-places, the winged mosquito population definitely increases again at about 22° or 23°C.

E. E. A.

ROUBAUD (E.). Un type racial nouveau de l'*Anopheles maculipennis*. [**A New Race of *Anopheles maculipennis*.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 737-740. With 2 figs. on 1 plate.

A previous paper by the author, with COLAS-BELCOUR and GASCHEN [see this *Bulletin*, Vol. 30, p. 305], referred to an experiment in crossing stenogamous males of *A. maculipennis* of Norman stock with large, eurygamous Dutch females. The Norman insects, originally found in the vicinity of Caen, and since maintained and studied in the laboratory for several years, are now considered to represent yet another race or variety of *A. maculipennis*, which is accordingly characterized in the present contribution as var. *fallax*.

The eggs of this new race, which are dark, dappled, and have broad floats, are of the *messeae* type. In details of egg-structure, although not in certain larval characters nor in the stenogamy of the zoophile, multidentate adults, var. *fallax* likewise approaches HACKETT's var. *melanoon*, the validity of which, however, cannot yet be regarded as established. The larvae of the Norman race show affinity with those of the *typicus-messeae* group in certain morphological details, although there are discrepancies in others. Further approximation to the *typicus-messeae* group is seen in the number and shape of the harpagonal spines in the males.

Similar affinities are displayed on the biological side, var. *fallax* being homodynamous and ready to breed at all seasons. The great difference is in its stenogamy, as a result of which it breeds readily in a cage one-twentieth of a cubic metre in size; in this respect alone it agrees with var. *atroparvus*. On a biological basis, the position of the subject of this paper among the races of *A. maculipennis* whose characteristics are definitely known may be shown as follows:—

*Homodynamous	{	eurygamous :	{ <i>labranchiae</i> .
			{ <i>typicus-messeae</i> .
		stenogamous :	<i>fallax</i> .
Heterodynamous :		stenogamous :	<i>atroparvus</i> .

E. E. A.

BEKLEMISHEV (W.). Ueber einige Gesetzmässigkeiten in der Larvenökologie von *Anopheles maculipennis*: das Optimum der Pflanzenabundanz. [The Larval Oekology of *A. maculipennis*: Influence of Vegetation.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 5. [In Russian pp. 361–376. With 4 figs. [26 refs.] German summary pp. 376–377.]

Deals in detail with the relations of *A. maculipennis* larvae to floating and submerged vegetation, discussing the favourable and unfavourable factors. A. G. B.

CORRADETTI (Augusto). Ricerche sugli incroci tra le varietà di *Anopheles maculipennis*. [Crosses between the Races of *A. maculipennis*.]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 6. pp. 707–720. With 4 figs on 1 plate. English summary.

“The results of crosses between the Italian *A. mac. atroparvus* and *A. mac. typicus*, *A. mac. messeae*, *A. mac. elutus* are first described. The males of the Italian *atroparvus* mate in confinement with the females of the other *maculipennis* races, but the reverse does not occur; furthermore, the crosses of the first hybrid generation are not fertile, owing to the high incidence of the atrophy of the testicles and ovaries. Then it appears that the behaviour of the Italian *atroparvus* in these crosses is the same as that of the Dutch *atroparvus*. From other researches, carried out on the crosses and re-crosses between *A. mac. labranchiae* and *A. mac. atroparvus*, it results that the eggs deposited by the F_1 generation show intermediate

*Although what the late Lt.-Col. ALCOCK once described as “the opulent terminology apparently inseparable from the subject” must by this time be fairly familiar to readers of papers on races of *A. maculipennis*, the combined effect of four of these formidable-looking terms in close order is somewhat overwhelming. A glossary is accordingly appended:—

Homodynamous, not subject to complete hibernation.

Heterodynamous, subject to complete hibernation.

Eurygamous, not mating in a confined space, but needing to make a nuptial flight as a preliminary to copulation.

Stenogamous, breeding freely in cages of very limited dimensions. E. E. A.

characters between the *labranchiae* and *atroparvus* eggs. According to Mendel law, the distribution of these characters are 75 per cent. for the dominant (*A. mac. atroparvus*) and 25 per cent. for the recessive (*A. mac. labranchiae*).

"If F_1 is eurygame or stenogame, has not been established; interbreeding (males and females of the F_1) fertile eggs have not been obtained.

"This negative result is difficult to explain; the males show normal testicles only in 10 per cent. of the cases.

"In the second generation obtained through the re-cross of the hybrid female with the *atroparvus* male, the stenogame character is dominant. For this reason interbreeding is possible. The eggs deposited are fertile; in 70 per cent. of the cases the males show normal testicles.

"The results of Roubaud and the Dutch authors on the possibility of crosses between the *atroparvus* females and *labranchiae* males are confirmed."

RAYMOND-HAMET. Démonstration expérimentale, sur l'animal entier, de l'action vasodilatatrice de la quinine. [The Vasodilator Action of Quinine Demonstrated in the Living Animal.]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 3. pp. 231-233. With 1 fig. [18 refs.]

Quinine was injected into the deep femoral artery of a vagotomized dog. The blood pressure and the flow of blood were measured. The blood pressure fell continuously with the escape of blood, but nevertheless the flow became twice as fast after the injection of quinine, owing to vasodilatation.
W. F.

BERNARD BEIG & CAUJOLLE (F.). Sur l'élimination de la quinine par la bile. [Elimination of Quinine by the Bile.]—*Bull. Acad. Méd.* 1935. Jan. 29. 99th Year. 3rd Ser. Vol. 113. No. 4. pp. 147-151. With 1 fig. [30 refs.]

A woman of 58 who had had a cholecystostomy with a resulting biliary fistula received intravenously a dose of quinine of 0.0034 gm. per kilo. Quinine appeared in the bile 15 minutes after the beginning of the administration. The author points to the importance of this observation owing to the large surface offered by the intestine for reabsorption. Details of technique are given.
A. G. B.

STOKER (W. J.). Over de malariagevaarlijkheid van *A. leucosphyrus*. [Malaria Infection Rate of *A. leucosphyrus* (Borneo).]—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Oct. 9. Vol. 74. No. 21. pp. 1342-1344. English summary (2 lines).

In the village of Sarang-Tioeng (Borneo) of 110 *A. leucosphyrus* examined 7 were found infected with malarial parasites (6.4 per cent.). A. G. B.

DE BUCK (A.) & SWELLENGREBEL (N. H.). Further Observations on the Pattern of the Upper Surface of the Ova in the Dutch Varieties of *A. maculipennis*.—Reprinted from *Proc. Acad. Sci. Amst.* 1934. Vol. 37. No. 8. pp. 578-579. With 7 figs. on 1 plate.

DE BUEN (Eliseo). Estudios sobre la biología del *Anopheles maculipennis* Meig. Índice maxilar y longitudes de ala, abdomen y tórax.—*Medicina Países Calidos*. Madrid. 1935. Feb. Vol. 8. No. 2. pp. 73-84. With 9 figs.

COUREL FERNÁNDEZ (Miguel). Memoria de la campaña anti-palúdica de 1932 en Castrelo de Miño (Orense).—*Rev. San. e Hig. Pública*. 1934. Nov. Vol. 9. No. 11. pp. 460-470. With 5 graphs & 1 fig.

FERREIRA (Barreto Gonçalves). Malaria no Recife.—*Folha Méd.* 1934. Oct. 5. Vol. 15. No. 28. pp. 329-331.

- GALLIARD (H.) & SAUTET (J.). Quelques caractères morphologiques d'*Anopheles elutus* de Corse.—*Ann. Parasit. Humaine et Comparée*. 1935. Jan. 1. Vol. 13. No. 1. pp. 1-4. With 2 figs.
- GIOVANNOLA (A.). Dopo 300 anni da una grande rivoluzione nel campo della medicina. La scoperta della china nella leggenda e nella storia.—*Riv. di Malariologia*. Sez. II. 1934. Vol. 13. No. 3 bis. pp. 169-174. With 2 figs. [10 refs.]
- GUY (R.). Note sur l'endémie palustre à Luang-Prabang (Haut-Laos).—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Oct. Vol. 12. No. 8. pp. 766-791. With 4 charts & 1 folding plan.
- . Quelques index d'endémicité palustre dans la Haute-Région laotienne (Luang-Prabang).—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Oct. Vol. 12. No. 8. pp. 792-806. With 1 map.
- HAMEL (J.) & CHAVAROT (M.). Contrôle de la guérison des impaludés thérapeutiques par la réaction de Henry.—*C. R. Soc. Biol.* 1935. Vol. 118. No. 1. pp. 93-94.
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- KIRK (Robert). A Case of Intra-Uterine Malarial Infection.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 421-424. With 2 charts.
- LEGENDRE (F.). Note sur une tournée de prospection antipalustre à Ambaton-drazaka et dans la région du lac Alaotra.—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 957-960.
- MARZINOWSKY (E.). Indice terapeutico en la infección palúdica.—*Medicina Paises Cálidos*. Madrid. 1935. Feb. Vol. 8. No. 2. pp. 104-105.
- MOREAU (P.). Notes sur un voyage d'études malariologiques dans l'Océan Indien. (Java.—Iles Mascareignes.—Afrique du Sud.)—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Aug.-Sept. Vol. 12. No. 7. pp. 674-703. With 6 figs. on 3 plates & 1 chart.
- NÄGELSBACH (E.). Malaria tertiana unter dem Bild eines Magendarmkatarrhes.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 126-127.
- PAOLO (Romby). Au sujet du pigment des parasites du paludisme.—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia* Milan. 1934. Nov. Vol. 6. No. 11. pp. 451-456.
- SCHWETZ (J.). Quelques considérations et réflexions sur l'immunité malarienne.—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 5. pp. 669-678.
- VAN SLYPE (W.). Sur la valeur curative et prophylactique de l'atébriane injectable.—*Ann. Soc. Belge de Méd. Trop.* 1934. Sept. 30. Vol. 14. No. 3. pp. 379-383.
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PLAGUE.

ESKEY (C. R.). **Epidemiological Study of Plague in the Hawaiian Islands.**—*Public Health Bull.* No. 213. Wash. 1934. Oct. 70 pp. With 6 figs. (2 maps).

PUBLIC HEALTH REPORTS. 1935. Feb. 22. Vol. 50. No. 8. pp. 255–257.—**Epidemiological Study of Plague in the Hawaiian Islands.**

In view of the tendency of plague to spread by sea-going vessels to distant ports the Hawaiian Islands, lying as they do on the trans-Pacific trade routes between North America and the Orient and Australia, have a special epidemiological importance. They are "The cross roads of the Pacific." A very complete study of plague in these islands is presented in this monograph: it contains many points of general interest in addition to those for official record.

The first case of plague occurred in Honolulu, December 12, 1899 and "the source could have been Hongkong or it could have been Japan." There followed on the islands 17 cases in December 1899, 35 in January 1900, 10 in February and 9 in March and so the epidemic was launched. Human cases have occurred every year since although, at the present time, they are very few in number. Two important epidemiological types of plague have been differentiated, the one of short duration where practically all cases occurred within towns or villages, the other long, persistent and occurring "on isolated rural premises" with a finding of infected rodents at great distances from buildings in fields and gulches. The two types are designated urban and rural respectively. A marked difference of the same order was found in the distribution of the two species of flea *Xenopsylla cheopis* and *X. hawaiiensis*. The latter was first detected on rats in 1932 and it has a similarity to the *X. astia* of Asia. Infestation of rats by fleas has a marked difference according as the rat is caught in or at a distance from buildings. Thus one table shows the *X. cheopis* index for female rats to be 3.57, 1.66, 0.5 and 0.26 respectively according as the host animal was caught inside building, under and within 50 ft. of building, 50 to 200 ft. and over 200 ft. from building. These indices may be contrasted with a series of similar figures for *X. hawaiiensis*, which were respectively 0.2, 0.35, 0.55, 0.87, 0.66, 0.86, 0.72 and 1.01 under the following conditions:—Inside building, under 25 to 100 ft. from building, 300 to 500 ft., 500 to 1,000 ft., and over 1,000 ft. from building. Therefore in the Hawaiian Islands *X. cheopis* infestation decreased with distance from buildings and *X. hawaiiensis* was more prevalent at a distance or on rats harbouring in fields and gulches.

Starvation survival of fleas is considered by many recent authors to be of great importance. The experiments here recorded showed that when *X. cheopis* were removed from wild rats none lived longer than 9 days while those collected from laboratory jars remained alive for 13 days. As regards the rôle of the fleas mentioned in the transmission of plague the author states that *X. cheopis* "were probably the infecting agents responsible for nearly all human cases" and that "epidemiological evidence indicates that *X. hawaiiensis* is the plague transmitting agent among field rats responsible for the endemic type of infection" in certain regions of the islands. There is a "native" rat as well as a native flea: it was described as *Rattus hawaiiensis* in 1917 and is closely related to the Malay rat, *R. concolor*.

Plague control measures are considered in the concluding pages of this monograph and are summarized as follows:—(1) "Rat proofing will eliminate the chief breeding places of *X. cheopis* as well as the rat population of buildings," but "rat proofing will not control endemic plague of field rats transmitted by *X. hawaiiensis*."

(2) "Trapping rats is a costly and ineffectual means of reducing the rat population especially of field rats."

(3) "Poisoned grains distributed in the form of paper packages . . . have proven to be a very safe method for using poison. . . . The attractiveness of grains may be enhanced by mixing them with coconut, bacon, or fresh fat, and other food stuffs. . . . Poisons have to be employed constantly or the rat population soon returns to its normal level." As poisons white arsenic in ten per cent. mixtures was used in field work and thallium sulphate in 5 gm. packages of a mixture of 3 lbs. to 1,000 lbs. of grain "in and near buildings, where there was the greatest danger of accidents occurring." W. F. Harvey.

- i. SAVINO (Enrique). Tres brotes pestosos en las provincias de Salta, Jujuy y San Luis. [**Three Outbreaks of Plague in Argentina.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Mar. Vol. 6. No. 2. No. 99–129. With 4 maps & 19 figs. English summary.
- ii. ——. Un nuevo brote de peste en Recreo (prov. de Catamarca). [**A New Epidemic of Plague in Catamarca.**]—*Ibid.* July. No. 3. pp. 295–303. With 6 figs. English summary (7 lines).
- iii. DE LA BARRERA (J. M.) & ARZENO (M.). Brote de peste en la prov. de Córdoba. [**Outbreak of Plague in the Province of Cordoba.**]—*Ibid.* pp. 330–341. With 6 figs. & 1 map.

i. The first of these outbreaks of plague, in which the majority of cases were pneumonic, probably took its origin from a case of secondary plague pneumonia in a child and was preceded by a rat epizootic. In the second epidemic the site of the plague was at 2,000 metres above sea level and was only accessible by a mule track, thus illustrating how plague may reach very isolated places by little frequented routes. The third outbreak arose from a rat epizootic in a grain shed, affected only the human population in the neighbourhood, and was bubonic in type.

ii. This is the third epidemic of plague which has appeared in the village of Recreo in the Argentine since 1920. Nine human cases of bubonic plague with 3 deaths occurred and there was the usual accompaniment of an epizootic. No trace of any epizootic, however, was found among wild rodents.

iii. This is an account of a small epidemic in the Argentine province of Córdoba comprising 15 cases of bubonic plague with a mortality of 46·66 per cent. The origin of the epidemic is not at all clear. Rats were numerous in the territory but were not found either dead or sick, nor was there much evidence of contact of wild rodents with man.

W. F. H.

URIARTE (Leopoldo) with the co-operation of Blanca CALCAGNO, Marcus RIESEL & Benjamin ANCHEZAR. Pulgas y peste. [**Fleas and Plague.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Mar. Vol. 6. No. 2. pp. 57–98. With 1 fig. & 12 plates (2 coloured). [Refs. in footnotes.] English summary.

Previous work on the infestation of rats by different species of fleas had shown that in Buenos Aires the percentage of *X. cheopis* was as

high as 95 per cent. More recent investigation (1927-1932) has brought down this high relative proportion by the inclusion of other species. A total of 30,389 rats was examined, of which only 722 (2·37 per cent.) carried fleas. The total number of fleas was 1,439 and the index (0·04 per cent.) was very low. Relative proportions of the different species, in percentages, were *X. cheopis* 61·25, *Ceratophyllus fasciatus* 31·54, *Leptopsylla segnis* 5·76, *Ctenocephalus felis* 0·66, *Ceratophyllus londiniensis* 0·26, *Pulex irritans* 0·2, *Craneopsylla wolffhugeli* 0·2. The last of these, which is ordinarily a parasite of a purely field rodent, was found on the rat for the first time.

W. F. H.

PERYASSÚ (Antonio). Peste. Determinação dos focos latentes de peste, pelo exame systemático de ratos, para verificação de portadores da "Pasteurella pestis." [**Systematic Examination of Rats to determine Plague Foci.**—*Brasil-Medico*. 1934. Mar. 17. Vol. 48. No. 11. pp. 190-191.]

Examination of rats in a plague area has shown that a certain number may be found infected as carriers, although presenting none of the usual gross characters of the disease. The finding of these, if the examinations are kept up in interepidemic periods, precedes the discovery of mild cases at the beginning of an epidemic. The recommendation of the author to examine all rats caught and to test their infectivity by inoculation has been carried out in Rio de Janeiro. During the past three years 45,151, 63,559 and 75,348 rats, have been examined and their livers and spleens inoculated into guineapigs. No rats were found infective by direct examination; of the guineapigs 875 died but none was found infected. Rio has been free from plague since the beginning of 1930, and no infected rats have been seen since July 26th, 1929.

In addition 1,492 rats from ships anchored in the harbour of Guanabara or in transit have been similarly examined, but none have been recorded as positive. The author concludes "Dealing with so large a number by direct examination and inoculation, we can guarantee the eradication of plague from our Capital Federal. This is an example of a sanitary measure which ought to be copied in the whole of Brazil."

H. H. S.

LONG (John D.) & MOSTAJO (Benjamin). Experiencias con pulgas como portadoras de peste bubónica. [**Fleas and Bubonic Plague.**]—*Bol. Oficina Sanitaria Panamericana*. 1934. Nov. Vol. 13. No. 11. pp. 1016-1024. With 1 map.

The authors state that bubonic plague was first introduced into the western coast of South America in April 1903, by way of the ports of Callao and Pisco, Peru. Since then there have been some 21,000 cases, or an average of 700 annually. It is significant that in the 37 Peruvian ports where plague has appeared, it has done so in places widely separated rather than in adjacent ports, in the wake of coastal vessels.

The infection appears to be conveyed in vessels with cargoes of jute and such like. They quote the case of s.s. *Solafric* from Calcutta in February with a cargo of 2,715 tons of bags, jute sacks and cordage; 2,911 bales were consigned to Peruvian ports, which she reached at the end of April 1933. They trace its calling places in Peru

and the appearance thereupon of plague rats and human cases.. A map shows the sequence clearly. Fleas found in the bales of jute were identified and the commonest were *X. cheopis*, others being *Leptopsylla musculi* and *Hectopsylla* in small numbers.

In their summary the authors conclude that cases of bubonic plague arising unexpectedly and out of season in Peru nearly always occur on sugar or cotton estates where a large amount of jute or other sacking is used and are due to "infection imported by fleas carried in cargos of jute," and that the recent appearance of the disease in the Canete valley and in Callao, Chimbote and Eten was due to such importation, while the same explanation would account for certain cases in Lima and its neighbourhood, although it has not been possible to determine accurately the spread of infection there.

H. H. S.

LÉGER (J. P.). Une saison de peste en brousse malgache. [A Season of Plague in the Bush in Madagascar.]—*Ann de Méd. et de Pharm. Colon.* 1934. July–Aug.–Sept. Vol. 32. No. 3. pp. 293–308.

This communication tells of the occurrence of plague which, owing to the burial customs and the habits of a primitive people, was able to reach considerable proportions before it was recognized. It was a more than usually severe epidemic and followed the usual rodent epizootic in rats of the *rattus* and *alexandrinus* type. A forest type of rodent, *Brachytaromys albicauda*, not yet described as subject to plague was one of those affected. Plague appears regularly in these bush regions in the hot season and disappears with the coming of the rains.

W. F. H.

ROUBAUD (E.) & MEZGER (J.). Présence à Madagascar de *Dinopsyllus lypus* J. et R. puce pestigène des rongeurs de l'Afrique du Sud. [Presence in Madagascar of *D. lypus*, a Plague-carrying Flea of S. African Rodents.]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 740–741.

The specimens which proved to be this flea were collected 200 km. from Antananarivo. Members of this genus have hitherto been met with in Uganda, Kenya and S. Africa, not in Madagascar. *D. lypus* infests a number of rodents [see this *Bulletin*, Vol. 30. p. 567], bites man, and experimentally transmits plague to gerbilles. Among 2,000 fleas collected in Madagascar only 15 were of this species. It is not known whether it transmits plague there.

A. G. B.

ARMSTRONG. Les événements épidémiologiques survenus du 1er juillet au 20 novembre 1934 [en A.O.F.]. [Epidemiological Events in French West Africa from July 1st to November 20th 1934.]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 952–953.

The account given of epidemiological events relates to plague, typhoid fever, diphtheria, dysentery, measles, leprosy, relapsing fever and trypanosomiasis. At Dakar the year was notable for the great frequency of pneumonic plague, 161 cases altogether, of which 61 were primary. It is interesting to note that prediction of the severity of the coming plague season was made at the beginning of the year and that this proved to be true. This prediction was based upon the density of

the murine invasion and the exceptional abundance of fleas. No correlation was found between meteorological features and plague frequency.
W. F. H.

GILMOUR (C. C. B.). **Bubonic Plague, Rats and Fleas in Singapore.**—*Malayan Med. Jl.* 1934. Dec. Vol. 9. No. 4. pp. 177–181. With 3 figs.

Plague has never become a menace in Singapore: the factors of transmission there are discussed.

It is now thirty years since plague made its first appearance in Singapore and that should be a sufficient length of time to take stock of the facts and “perhaps draw conclusions.” The facts in this article are taken from the Annual Reports of the Municipal Officer of Health of Singapore and from observations in the laboratory. There have been 712 deaths representing the very high mortality of 93 per cent. and these were distributed as follows:—Chinese 605, Indians 120, Malays 24, other nationalities 15. And yet, in spite of the high mortality plague has had no significant effect on the general death rate of the town. Climatic conditions deserve the name of “equable” in Singapore, for the mean temperature hardly varies at all throughout the year, humidity shows little variation and there are no seasons. Plague cases have occurred in every month of the year for thirty years, but there is a close correlation between human plague and wet weather. The predominant rat in the town is *M. decumanus* and the predominant flea *X. cheopis*, but more fleas are found on *M. rattus* than on *M. decumanus*. The flea index is low and during late years especially so. Several graphs and tables are given, the first of these being that of plague cases from 1901 to 1929. A low plague rate is manifest for at least the last three of these years. A suggestion is made by the author that ants may help to keep down the flea population. W. F. H.

GRIKUROW (W.). Zur Frage der Aufbewahrung des Pestvirus im endemischen Herd während der interepizootischen Periode. [On the Preservation of the Plague Virus in an Endemic Area during the Inter-Epizootic Period.]—*Rev. Microbiol., Épidémiol. et Parasit.* 1934. Vol. 13. No. 3. [In Russian pp. 207–211. German summary p. 211.]

With a view to establishing the causes of endemicity in a plague area, observations were conducted on the susliks [*Citellus pygmaeus*] inhabiting twelve areas of 9 hectares each in a district of Northern Caucasus. The rodents which survived the summer epizootic (1932) were left unmolested till next spring (1933), when 450 of them were caught and isolated for further observations. Most of the animals perished in captivity without showing any symptoms (clinical and bacteriological) of plague infection. However, in one individual *Past. pestis* was isolated in culture, which produced a typical fatal infection in a control animal. It is concluded that during the interepizootic period the infection is latent in the body of the susliks and various factors, such as exhaustion and other conditions, provoke a generalized infection which ultimately gives rise to a plague epidemic in the suslik population.
C. A. Hoare.

DOBRADIN (P. M.) & SKORODUMOV (A.) [Edited by]. [Collected Works of the Anti-Plague Organization of the Eastern Siberian Region for 1929-1931.] [Trans. East Siberian Reg. Inst. of Microbiol. & Epidemiol. Irkutsk. 1933. Vol. 1. 120 pp. With 10 figs. & 3 charts. (In Russian.)]

The anti-plague organization of Eastern Siberia is concerned with co-ordinating the work of the various laboratories and stations scattered throughout the region. The present volume comprises reports of the activities of these institutions (between 1929 and 1931) and a number of special articles among which the following may be noted.

V. V. SHUNAEV (p. 42) records the results of an experimental infection of a hibernating tarabagan (*Arctomys bobac*) with *Past. pestis*, resulting in the formation of a cutaneous plague ulcer which persisted until the death of the animal two months later. The chronic course of the infection serves to elucidate the origin of the early spring outbreaks among rodents and human beings. The same author (p. 43) failed to infect a wolf *per os*, while hares were found to be susceptible. V. L. PETROVSKY (p. 45) describes a case of spontaneous plague in a polecat (*Putorius eversmanni*), probably acquired by feeding on infected rodents. SHUNAEV (p. 50) tested the viability of the plague bacillus under winter conditions by placing drops of a two-days' culture of *Past. pestis* on pieces of cloth and exposing them in sterile Petri dishes to temperatures varying between -10° to -47°C . Cultures taken from this material 45 days later remained infective to guineapigs. A. M. SKORODUMOV (p. 51) tested the effect of freezing and thawing upon the virulence of the plague bacillus in cultures and in animal corpses, by subjecting them to the influence of the external temperature during the winter months. The bacilli retained their virulence for periods from 3 to 5½ months.

PETROVSKY (p. 55) determined the localization of *Past. pestis* in the organs of experimentally infected tarabagans. When inoculated subcutaneously the bacilli appear in the lymph glands from the fourth day; when introduced intraperitoneally they appear in the spleen, liver, kidneys and testicles on the third day, whereas they could not be isolated from the blood until the sixth day; after inoculation through the abraded skin of the abdomen the appearance of the bacilli in the parenchymatous tissues is delayed till the eighth day. P. N. BEKRENEVA (p. 60) devotes a paper to the distribution of the plague bacillus in the body of a vole, *Microtus brandti*, after subcutaneous inoculation. The bacilli first penetrate into the nearest lymph gland whence they find their way into the blood and are carried into the spleen, lungs, intestine and kidneys. The occurrence of these micro-organisms in the urinary bladder, in the faeces and in the urine indicate the method by which they are discharged into and contaminate the external medium. A. M. SKORODUMOV and L. A. MITCHURINA (p. 72) describe the effect of pyocyanin and rivanol upon plague cultures and experimentally infected guineapigs. Both drugs have a bactericidal action *in vitro* in dilutions of 0.01 and 0.02 per cent. However, their therapeutic and prophylactic effect in animals is negligible. SKORODUMOV (p. 79) describes a method for the differential diagnosis of *Past. pestis* and *Past. pseudotuberculosis rodentium*. When grown on nutritive agar media containing 0.3 per cent. Congo red and various sugars or glycerine, the two bacilli produce colonies differing in colour

and appearance. I. G. IOFF and A. M. SKORODUMOV (p. 88) give a description and list of the fleas found on animals in the endemic plague area of Transbaikalia. C. A. Hoare.

WILLIAMS (A. W.). **Some Unusual Forms of Plague.**—*East African Med. Jl.* 1934. Oct. Vol. 11. No. 7. pp. 229–232.

In an area where bubonic plague is endemic, and where, consequently, pneumonic or septicaemic plague can occasionally occur there is always the liability of admission of unsuspected cases to hospital. That is highly dangerous for fellow patients, when the case is one of pneumonia. "In any blood infection the clinical picture varies according to the system on which the brunt of the infection falls—hepatic, pulmonary, meningeal—a fact well illustrated by the records of these five cases." The five patients were admitted with symptoms resembling (1) toxic jaundice of yellow fever type, (2) primary meningitis, (3) pneumonia with delayed resolution and recovery, (4) in two cases, lobar pneumonia. The lesson to be drawn from such occurrences is that the sputum of all cases resembling pneumonia ought always to be examined for *P. pestis* whenever an outbreak of plague occurs or in an endemic area, as soon as the patient presents himself for admission. W. F. H.

GIRARD (G.). Technique simple et pratique de prélèvements pour identification du bacille pesteux chez l'homme. Son application au dépistage de la peste à Madagascar. [**Simple Technique for Diagnosis of Plague.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 32. pp. 601–603.

A simple technique for diagnosis of plague with material sent from a distance has been tested by the author. In the case of a patient the bubo is repeatedly punctured with a syringe, which is well washed out after each puncture with sterile normal salt solution. In the case of a dead body the same procedure is gone through, but it is the lungs or liver which are punctured. A suspension is obtained from the washings and this is inoculated by friction on the shaved and scarified skin of the guineapig. Material obtained 3 to 10 hours after death in the animal experiments was capable of causing acute plague, up to a minimum of 6 days, when kept at a temperature of 16° to 26°C. If kept at 37°C. the infective period was reduced to 3 days. If the animal had been dead 48 hours (local temperature 21°C.) and putrefaction had set in, the suspensions were only virulent for 24 hours, the organs for 3 days. These animal experiments have been confirmed in actual practice with material sent to the laboratory from distant parts. W. F. H.

KIRSCHNER (L.). Gal als voedingsbodem bij de diagnose der pest septicaemie. [**Bile Nutrient Medium in the Diagnosis of Plague.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Aug. 28. Vol. 74. No. 18. pp. 1141–1159. With 1 chart. [31 refs.] [Summary appears also in *Bulletin of Hygiene.*]

Bile has now for a long time been used to obtain pure blood cultures of typhoid group bacilli, while the bile salts have also been employed in the further process of purification. The author has applied similar procedures to the cultivation of the plague bacillus from blood or pus and found them successful.

It was already known that a septicaemia exists in the first three days of bubonic plague and is also found one or two days before death. After the addition of blood to bile (1 in 2 up to 1 in 100), or as the case may be pus (1 in 10 up to 1 in 100), an inoculation of a very small number of plague bacilli (10 to 40 per cc.) gave a good growth. The bile may be sterilized either by filtration or by heat (20 minutes at 110°C.) and the addition even of one drop of blood to 5 cc. bile is sufficient to show up a light septicaemia. From this preliminary culture inoculations may be continued upon ordinary agar, Endo, or Drigalski agar. The original bile inhibits the growth of cocci and the components of the continuation media inhibit the growth of cocci and *Proteus* bacilli. By the use of this enrichment method the author was able with a single trial to demonstrate a bacteraemia in 212 out of 237 definite plague cases. W. F. H.

MADRAS. Report of the Director of Public Health for 1933 [HESTERLOW (A. M. V.), Acting Director].—169 pp. 1934. Madras: Govt. Press. [pp. 42–45, paras. 76–79. **Plague Research**; pp. 45–46, paras. 80–82. **Research on Bacteriophage.**]

Work of considerable importance is shortly described under the heading of plague research in the Cumbum Valley, *e.g.*, the infectivity of starved fleas; climatic conditions in rat burrows; value of bacteriophage.

Definite evidence of smouldering epizootics all the year round was found for some of the larger villages. This perpetuation is ascribed to the persistence of infection in rat fleas, even under conditions of deprivation of food for over four weeks. Wild rodents prevalent in the Cumbum Valley are moles of the species *Gunomys* Kok, gerbils, field mice, bush rats, bandicoots and house mice but although many of these have been proved to be very susceptible to plague they were not found to be naturally infected to any extent. Special stress has been placed on a research into the longevity of plague-infected rat-fleas under natural conditions in model houses. In the first of these experiments a positive transmission was obtained after continuous starvation for 63 days, while in the third experiment infected fleas transmitted their infection even after periods of starvation of 6, 14, 22 and 29 days. Seven instances were found in this experiment of resolving plague in the test-rats, and this suggests the possibility that the bacillus had lost virulence with starvation of the carrier flea. Another point of importance for possible carry-over plague conditions is to be found in the climate conditions in rat-burrows. A special thermograph was used for record and it was shown that although the outside temperature might vary from 86.5°F. to 63°F. the temperature within the burrows ranged only from 79°F. to 72°F., thus proving how little the temperature in these burrows was affected by external diurnal variation. Again it was demonstrated "that a fairly uniform high humidity is maintained in rat-burrows, while the outside atmosphere shows wide variations."

In summary of these facts it may be stated "that the rat-burrow provides optimum facilities for plague infection in fleas to tide over the unfavourable hot months." A further research was directed to the value of cyanogas fumigation of rat-burrows in the prevention of plague. The evidence afforded is strongly suggestive of value and especially in the case of Cumbum village itself "which has remarkably escaped

human plague. . . . Prompt fumigation . . . arrested the course of epizootic plague and thus prevented the outbreak of human plague."

Bacteriophage research in cholera has not yielded clear-cut results. The conclusions arrived at are:—(1) The prophylactic administration of bacteriophage has not been shown to be effective in reducing the rate of attack. (2) The prophylactic administration of bacteriophage seems to lessen the mortality rate. (3) It has not been shown that bacteriophage is more useful than pro-diarrhoea mixture in the treatment of cholera."

W. F. H.

GIRARD (G.) & ESTRADE (F.). Nouvelle observation de peste dans un élevage de lapins et de cobayes consécutive à une épizootie murine. [Plague among Rabbits and Guineapigs of a Breeding Establishment following a Rat Epizootic.]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 962–963.

On the 8th June there were brought to the laboratory of the Pasteur Institute two rabbits, which had died in their hutch. Next day a guineapig from the same place was brought and this was the only survivor of 15 animals. It died within 24 hours. The autopsy, examination of liver and spleen smears, the inoculation of guineapigs, and the identity of the culture in the case of all three animals led to the conclusion that the infection was plague and not a pasteurellosis nor pseudo-tuberculosis. It was found that a dead rat had been discovered in one of the animal hutches on the 29th May, three more on the next day and seven on the 1st June. Then the guineapigs began to die and after that the rabbits. The dead rats discovered were 17 in all. It was not till the 7th June that the proprietor became uneasy and informed the health authorities. By this time only one decomposed carcase of a rat was available and, as was expected, the result of test with it was negative. Nevertheless there seems little doubt on the evidence that the epizootic, occurring as it did in one of the oldest centres of plague, was itself one of plague.

W. F. H.

LIPATOVA (T.). Immunological Studies on Plague. III. Thermo-precipitin Test and Elaboration of the Method of obtaining Specific Precipitating Plague Sera.—*Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 3. [In Russian pp. 201–206. [13 refs.] English summary p. 206.]

The anti-plague serum obtained by immunization of horses with the live cultures of *Past. pestis* produces a group precipitation with *Bact. coli*, *Past. pseudotuberculosis rodentium*, *Proteus*, *Bact. paratyphosum A*, *Bact. paratyphosum B*, which accounts for the precipitation by anti-plague serum of thermo-extracts from the organs of animals which died from causes other than plague. Saturation of the anti-plague serum with the thermo-extracts of all the above-named organisms removes from it the group antibodies for these bacilli. If the anti-plague serum is saturated with one of the filtrates it is thereby freed of the group antibodies homologous to all the organisms used in the experiment. On account of the close serological affinity between *Past. pestis* and *Past. pseudotuberculosis rodentium*, the latter should not be employed for saturation, especially since saturation with the thermo-extract of *Bact. coli* destroys the antibodies for *Proteus* and causes a marked diminution in the antibodies for *Past. pseudotuberculosis rodentium*.

The sera exhausted by one or several filtrates produce precipitation with the thermo-extracts from the corpses of animals experimentally infected with plague, but not with those from the corpses of non-infected animals.

C. A. Hoare.

MINERWIN (S. M.), STUPNITZKI (P. N.) & TINKER (J. S.). Die Antipestvakzinen A-D. [**The Plague Vaccines A-D.**].—*Zent. f. Bakt. I.* Abt. Orig. 1935. Jan. 15. Vol. 133. No. 3/4. pp. 170-175.

Six types of vaccine were used in these trials and two species of animals, the ziesel mouse and the guineapig. The types were (1) dead and attenuated living, (2) salt and sugar bacterial suspensions, (3) virulent and avirulent plague organismal vaccines. Naturally only the avirulent strain was used for those vaccines in which the organisms were still living. A strain called No. 630 supplied the virulent and one called AMP the avirulent organisms. The special solution for sugar-suspension vaccines contained 150 parts of saccharose to 100 parts by weight of distilled water. A marked difference in the efficacy of the different types of vaccine was manifest, which was more or less the same for the two species of animals used. The results, expressed as percentage mortalities in ziesel mice, were for AMP salt, AMP sugar, AMP living, No. 630 salt, No. 630 sugar, and controls 57, 18, 18, 62.5, 25.5 and 75 respectively and the numbers of animals used in each category 14, 11, 11, 8, 12, and 12 respectively. Thus the sugar vaccines consisting of dead organisms and the attenuated living vaccine gave much the best results.

W. F. H.

ALBORNOZ (Francisco). Importancia de la desratización permanente y el saneamiento en la profilaxis de la peste bubónica. [**Importance of Permanent Deratization and Sanitation in the Prophylaxis of Plague.**].—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. July. Vol. 6. No. 3. pp. 304-329. With 35 figs. & 1 chart.

The port of Rosario, says the author of this article, has the distinction, if it may be called so, of having been the first place in which plague manifested itself in the Argentine. No case of the disease had occurred up to 1899. A vigorous campaign has been initiated in the last few years, of which the special features have been:—(1) Permanent deratization; (2) Employment of a specialized personnel; (3) Fixation of the personnel in each locality instead of the use of a flying squad; (4) Practice of an intense and permanent sanitation. Numerous illustrations are given of the methods used and the obstacles which had to be overcome. A most instructive graph of morbidity and mortality concludes the article and, with its testimony to the plague condition prevailing from the years 1927 to 1930 and the reduction of both these characters practically to zero during the years 1930 to 1934, is eloquent of the effect which may reasonably be supposed to have resulted from the measures adopted.

W. F. H.

DEPRAT. Peste bubonique et dératisation. [**Bubonic Plague and Deratization.**].—*Ann. d'Hyg. Pub., Indust. et Sociale.* 1935. Feb. Vol. 13. No. 2. pp. 78-100.

The author, who has had a long experience of plague from 1902 to 1927, both in practice and as port health officer of Rio Grande, here

expounds his views on the value of deratization as an anti-plague measure and questions current beliefs.

From the scientific investigations set on foot by the outbreak of plague at Hongkong in 1896 there has grown up the established doctrine that a rat epizootic is antecedent to the human epidemic and that transmission from the rat to man is effected by the agency of the flea. This doctrine has become the keystone of the arch of international sanitary defence against the scourge of plague. Deratization has been preached for 30 years as the sanitary safeguard against plague and as a specific international defence. But one may at the present time question whether this has not been a premature generalization on the experimental evidence of the possible transmission of plague from rat to rat by the flea. The demonstration of the transmission has not been made for the case of rat to man. This argument is developed throughout the article by the abundant citation of examples minimizing or negating the evidence of the major part played by the rat and its fleas in transmission of plague to man. The foundations of the supposition are regarded as insufficient or at least as not excluding other means of propagation. Constant new importation of plague from the Argentine to Rio Grande and particularly through the agency of grain, without its ever becoming endemic and quite independent of any measure of sanitary defence, is one of the negative instances insisted on by the author out of his own experience. His conclusions stress the point of our ignorance upon essential points concerning the epidemiology, the prevention and the treatment of plague.

W. F. H.

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- GIRARD (G.) & ROBIC (J.). Vaccination contre la peste au moyen d'une souche de bacilles de Yersin vivants, de virulence atténuée.—*Ann. de Mtd. et de Pharm. Colon.* 1934. July-Aug.-Sept. Vol. 32. No. 3. pp. 285-292.
- HUSSEIN (Abdel Gawad). Bubonic Anthrax simulating Plague.—*Jl. Egyptian Public Health Assoc.* 1934. 9th Year. Oct. pp. 25-26.
- KHAMBATTA (Kershaw D.). Plague in Poona City in 1933.—*Bombay Med. Jl.* 1934. July. Vol. 3. No. 7. pp. 189-191.
- URABE (K.). Species and Distribution of Mice in Mukden and Hwai-te. Studies of Animals connected with the Carrying of Plague. (Part I).—*Jl. Oriental Med.* 1934. Sept. Vol. 21. No. 3. [In Japanese pp. 303-320. With 10 figs. on 2 plates. [22 refs.] English summary pp. 25-26.]
- URIARTE (Leopoldo) with the co-operation of Blanca CALCAGNO, Marcos RIESEL & Benjamin ANCHEZAR. Pulicidés murins de Buenos Aires.—*Folia Biol. Buenos Aires.* 1934. June, July & Aug. Nos. 39-40-41. pp. 179-180. [A French summary of the paper noticed on p. 447 above.]
- URIARTE (Leopoldo). Acerca de la peste bubónica en la Argentina.—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Nov. Vol. 6. No. 4. pp. 446-457.
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CHOLERA.

DOORENBOS (W.) Etude sur le vibron cholérique. *Vibrio cholerae* typus épidémicus et *Vibrio cholerae* typus endémicus. [**The Cholera Vibrio. Epidemic and Endemic Types.**].—120 pp. 1934. Alexandrie : Société de Publications Egyptiennes.

There is no want of clarity in the views held and expressed by the author. He maintains that most if not all of the variants of the cholera vibrio, denominated para- or pseudo- cholera, are simply cholera vibrios. There is a definite epidemic cholera vibrio which, however, has no long existence in an epidemic before it ceases to maintain its peculiar serial cholerigenic character and becomes a "modified" vibrio. There is no such individual as a chronic carrier of the epidemic cholera vibrio but there are carriers of the modified cholera vibrio. These latter vibrios may be cholerigenic but not in series. They may account for sporadic cases.

In this way the author leads up to his classification of cholerigenic vibrios into the two great classes, the epidemic and the endemic. The modified cholera vibrio does not possess all the characters of the epidemic vibrio. It may or may not be agglutinable; it may be haemolytic; it may be otherwise modified. The agent which is most potent in modifying the epidemic cholera vibrio is the bacteriophage. It is by the action of bacteriophage that epidemics come to an end and the epidemic vibrio comes to its modified avirulent form. These views have a most important bearing upon the epidemiology of cholera especially on the meaning to be attached to the phrasing used in art. 29 of the International Convention of 1926; "Cases presenting the clinical symptoms of cholera . . . in which vibrios without the characters of the cholera vibrio have been found must be subjected to all the measures laid down for cholera." The same importance attaches to art. 101 of the new regulations adopted in 1934 by the Conseil Sanitaire Maritime et Quarantenaire of Egypt which couples together for quarantine purposes the "vibron cholérique" and the "vibron suspect," until the bacteriologist has pronounced the latter not to be a cholera vibrio. This pronouncement ought to be exact and furnished as rapidly as possible.

The memoir of the author is concerned with the two types of vibrio, the virulent epidemic type and the avirulent endemic type. It is not possible briefly to summarize the argument but some of the salient points may be touched on.

Quarantine for cholera is a disagreeable necessity for pilgrims and travellers. This was made especially prominent by the action of the sanitary authorities in Syria who examined very carefully travellers from Iraq at the time when Iraq was in the throes of an epidemic. This resulted at the beginning in the discovery of some 30 per cent. of carriers of vibrios, 12 per cent. of whom were carriers of true cholera vibrios. A great deal of research into the question of the cholera carrier has been made at the quarantine camp of Tor and controversy regarding the nature of the El Tor vibrio continues almost as vigorously to-day as it did after its first discovery in 1905. Transformation of vibrios, as will have been gathered from the opening summary, makes

up a good deal of the text in this monograph. We find that the author has seen agglutinating El Tor vibrios lose their agglutinability and vibrios which did not agglutinate become agglutinating El Tor vibrios. This famous vibrio is relegated to the category of a modified avirulent cholera vibrio. Much unanimity exists at the present day on the importance of agglutinability in the identification of the cholera vibrio, and yet we are told not to forget that "the choice of the agglutinating vibrio as the only true cholera vibrio" was in the first instance "an arbitrary choice and that the consequences of that choice are imposed upon us up to the present day."

Although D'HERELLE was the first to observe that cholera vibrios could undergo important modifications under the action of bacteriophage, the present author considers that he went beyond his facts in postulating that this modification was irreversible. One of the difficulties of such an association was to account for the preservation of the vibrio in nature. "It is more logical to admit that the cholera vibrio does not exist in nature in its ultra-pure and stable form but as a modified form which is more or less resistant to the bacteriophage and which can reacquire its original characters and its virulence when external conditions are favourable." This leaves the portal open, so to speak, for a return to biochemical, biological, cholorigenic and still further to epidemic characters. The characters of the epidemic or ultrapure strain are that it shows no gross contamination with bacteriophage, possesses a uniformity and regularity of biological characters and is homogeneous and stable. Cholorigenic power is dependent upon enterotropic character and this character is developed in high degree in the epidemic cholera vibrio. The endemic cholera virus is preserved in chronic carriers and is the ultimate source of recurrent epidemics, for the epidemic vibrio, although it is the homogeneous, stable, equilibrated form, cannot exist as such except for a very short space of time. Its epidemic existence is terminated by bacteriophage action and it returns once more to the dysequilibrated avirulent endemic type or state.

As the cholera carrier is the important personage from a quarantine point of view it is essential to know exactly how dangerous such carriers are and we have referred to the author's view that chronic carriers of the epidemic vibrio do not exist. We may add that the chronic carrier of endemic modified vibrios can give rise only to sporadic isolated cases of cholera; it is the epidemic carriers in the stage of incubation of the disease who alone, as travellers and transmitters of virulent virus into an epidemic focus, present any really great danger to other populations. A final quotation would seem to put the question reasonably clearly although it is not a solution of the quarantine problem. "If we admit that the epidemic virulent vibrio does not lend itself to transport of a prolonged character and that the endemic vibrio, which does so, is usually avirulent, it is also necessary to admit that the carriers of vibrios are only dangerous for the propagation of cholera under very special conditions." We are left here presumably to the use of our own judgment as to the action which should be taken regarding carriers, but we are assured in conclusion that the sanitary measures applied to pilgrims during their stay at Tor and the systematic investigation of vibrio carriers offer sufficient guarantees for prevention of transportation of the virus of cholera into Egypt and into Europe.

W. F. Harvey.

OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE, PARIS. **Report of the Cholera Commission to the Permanent Committee of the Office International d'Hygiène Publique. October Session 1934.** [M.S. copy received from the Ministry of Health, London.]

The first subject considered by the Commission was the preparation of a dried standard "O" cholera antigen for use in obtaining a high titre diagnostic serum. In such dried form the antigen could be despatched to all parts of the world and enable workers "to obtain exactly comparable serological results." The most suitable strain of the cholera vibrio to be used has still to be determined.

A very important decision was taken by the Commission with regard to the El Tor vibrio and haemolytic cholera-like vibrios generally. It amounted to a re-affirmation of the *status quo ante*, which is that these cholera-like vibrios even if they agglutinate with true cholera serum are not true cholera vibrios. This pronouncement has reference to a note presented by Dr. DOORENBOS, the delegate for Egypt [see above]. It is set out briefly as follows:—

(a) The vibrios obtained from pilgrims at Tor are not considered to be true cholera vibrios, inasmuch as they may differ from that vibrio in haemolytic properties, bacteriophage resistance, etc., even if they possess certain serological characters of true cholerigenic vibrios. "It has not been shown," moreover, "that they are capable of producing cholera," nor does reversibility of characters prove identity.

(b) The separation of cholera vibrios into two types, with the nomenclature of *V. cholerae typus epidemicus* and *V. cholerae typus endemicus* and all its implications, is not advisable.

(c) Further evidence is required before acceptance of a specific source of contamination of pilgrims in the Hejaz. W. F. H.

GHOSH (H.). **Treatment of Cholera with a New Anti-Cholera Serum.** Preliminary Note.—*Brit. Med. J.* 1935. Jan. 12. pp. 56-57.

By anaerobic culture for 18 hours in special broth (this *Bulletin*, Vol. 30, p. 538) a toxic filtrate had been obtained which was capable of producing, by repeated small intravenous doses in rabbits, a cholera-like diarrhoea. Horses have been immunized with this toxin in doses as high as 500 cc. The serum obtained, when concentrated afforded an agglutinating titre of 1-12,000 "H" agglutinin and 1-1,600 "O" agglutinin. "A previous injection of serum prevented experimental production of cholera diarrhoea with the toxin in laboratory animals." Now the opportunity has occurred of testing the serum in human beings. By intravenous injection the serum did not prove entirely satisfactory except in mild cases of cholera. The author then adopted the intra-peritoneal route of administration in a dose of 30 to 40 cc. serum, diluted with 200 cc. warm normal salt solution. A single saline transfusion was given on admission of a patient and then the serum. The results obtained in a limited series of cases were:—4 deaths in 32 treated with serum and 15 deaths in 57 cases treated without serum.

W. F. H.

RAYNAL (Jean). Etude des bactériophages appliqués à la prévention du choléra dans les Indes anglaises. [**Study of the Bacteriophages used for the Prevention of Cholera in British India.**].—*Rev. d'Hyg. et de Méd. Préventive*. 1934. Nov. Vol. 56. No. 9. pp. 669-690. With 2 figs. (1 map.)

This communication is the report of a mission specially detailed to "study in the bacteriological laboratory of Shillong in Assam the technique of preparation of bacteriophages and their practical application to the prevention of cholera." A large-scale experiment has been going on for some years now under Colonel MORISON and his co-workers [see this *Bulletin*, Vol. 31, p. 891], which has attracted wide attention to the possibilities of phage in cholera and incidentally added to our knowledge of the action of phage. It is the striking result obtained in this trial and the evidence of what would appear to be a circumstantially controlled experiment which challenge and demand the verdict of all workers in preventive medicine. The French mission has not been content to read of these results but has journeyed to see them. In the article by the author we have set out, map, graph and table with full description of technique and a running commentary on what he heard and saw. An excerpt therefore from his final conclusion makes interesting, though somewhat disappointing, reading: "We are led therefore to conclude," says the writer, that "the whole question of anti-cholera bacteriophage, as well as the technique of its preparation are not yet definitely settled. It is difficult to be certain yet of the value of prophylactic methods for cholera founded upon the use of bacteriophage. . . . It is advisable still to await the result of the anticholera campaign with bacteriophage before passing judgment on its value. Nor is it at present desirable to replace the tried methods of prophylactic vaccination with anticholera bacteriophage. . . . Cholera is a disease in the presence of which one feels helpless. But the bacteriophage has given encouraging curative results. It would seem quite reasonable then to make a beginning with bacteriophage therapeutically. For this purpose it would be necessary to use bacteriophages which have been recently isolated at the time of an epidemic and which possess a high lytic activity on a large number of autochthonous cholera vibrios."

W. F. H.

MORISON (J.), RICE (E. Milford) & HAYTHORNTHWAIT (R. A.). **Bacteriophage, Essential Oils and Vaccination and their Effects on Cholera Mortality.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 317-339. With 3 graphs.

The argument developed in this article is in favour of the use of bacteriophage treatment of cholera as against vaccination of contacts and treatment of cases with essential oils. Two areas came under consideration, represented by parallel and adjacent valleys. Numerous tables and graphs are given of the data. The results are somewhat difficult to assess, in the absence of a summary of formal conclusions.

W. F. H.

RAJA (K. C. Kutty Ettan). **The Use of Bacteriophage against Cholera in North Arcot District, Madras Presidency, in 1933.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 397-424.

A trial of bacteriophage has been instituted by the author from the Public Health Department of Madras. Some villages were taken as

controls and others selected for distribution of 'phage. In both groups, however, the usual methods for dealing with cholera were adopted including anti-cholera inoculation but in the test villages oral administration and addition to wells of 'phage were also carried out. Both the discussion and the conclusions make it appear that no satisfactory evidence was forthcoming for the efficiency of the 'phage used. We may, however, note the remark of the author that :—" It has to be emphasized that the figures dealt with in this report are small and that, therefore, it is unsafe to draw definite conclusions." W. F. H.

DAMBOVICEANU (A.) & SORU (E.). Action *in vitro* du bactériophage sur les propriétés des vibrios cholériques. [**Action of Bacteriophage in Vitro on Cholera Vibrios.**]-C. R. Soc. Biol. 1934. Vol. 117. No. 29. pp. 295-297.

Much attention is at present being devoted to the antigenic complexity of micro-organisms and especially of the cholera vibrios. The authors have investigated the changes in antigenic constitution of vibrios acted on by phage and summarize their results as follows :—(1) All the true cholera vibrios, both the smooth forms and those which are primarily rough before the action of bacteriophage, furnish extracts rich in residual antigen. (2) Vibrios which, being originally smooth, have become rough under the action of bacteriophage *in vitro*, no longer give any residual antigen. (3) Mixtures of smooth and rough furnish, after action of bacteriophage, extracts which are extremely poor in residual antigen. (4) Lastly, if the vibrios have been long in possession of rough characters, whether this has been before or after the action of bacteriophage, they provide extracts very rich in residual antigen.

W. F. H.

LINTON (Richard W.) & MITRA (B. N.). **Studies on the Antigenic Structure of *Vibrio cholerae*. Part VII. Two Acid-Soluble Protein Fractions.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 295-308.

In the last of these studies [this *Bulletin*, Vol. 31, p. 893] the protein composition of cholera and cholera-like vibrios was studied and two proteins, I and II, found to be present. In this continuation study two acid-soluble protein substances, "A" and "B," have been isolated from cholera, cholera-like, smooth, smooth-rough and rough vibrios. "A" comparison of all the chemical findings indicates that the 'A' substance is very similar from whatever type of strain or protein it is extracted. 'B' substance differs markedly from 'A,' but again is the same irrespective of source." "B" appears to be closely allied to residual protein after acid extraction and also to "whole protein." W. F. H.

GARDNER (A. D.) & VENKATRAMAN (K. V.). **The Antigens of *Vibrio cholerae*.**—*Lancet*. 1935. Feb. 2. p. 265.

A large group of vibrios exists with the same cultural and biochemical reactions as the *Vibrio cholerae* and the same heat-labile or H. antigen. This group is capable of subdivision on the basis of differences in heat-stable or O antigens. Agglutination and absorption tests with O sera are largely used for differentiation. A condensed preliminary account is here given of an examination of the Japanese subdivision into their

original, middle and variant types, with confirmation of the reality of the first and third. The table published shows that "the Japanese type differences are in no way confined to Japanese vibrios. Races from India, China and elsewhere show the same variations of their subsidiary O antigens and even among the haemolytic vibrios from El Tor (Dr. Doorenbos) those that fall into the same O subgroup as the classical cholera vibrio (by no means all of them do so) show the same kind of variation."

W. F. H.

UYEDA (Saburo). **Local Skin Reactivity to the Culture Filtrate of *Vibrio cholerae* as demonstrated by Shwartzman Phenomenon.**—*Acta Scholae Med. Univ. Imperialis in Kioto*. 1934. Vol. 17. No. 2. pp. 146–158. With 3 figs. on 1 plate. [15 refs.]

According to SHWARTZMAN if rabbits which had been injected intracutaneously with a filtrate of *Bact. typhosum* received 24 hours later an intravenous injection of the same filtrate, there developed at the site of the previous injection a severe haemorrhagic necrosis. Later work showed that the necrosis could be produced by filtrates of other than the specific organism. The phenomenon was therefore not strictly specific. The author has used filtrates of *V. cholerae*, produced the phenomenon and again found it to be non-specific.

W. F. H.

LINTON (Richard W.), SHRIVASTAVA (D. L.) & MITRA (B. N.). Notes on the Structure of the Cholera and Cholera-like Vibrios.—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 309–312.

REVIEWS AND NOTICES.

IOFF (I. G.). [**Memorandum on Anti-Malarial Campaign in Collective and Soviet Farms.**].—104 pp. With 6 text figs. (In Russian.) 1934. Rostoff-on-Don: Published by the Azov-Black Sea Regional Tropical Institute. [Price 50 kopecks.]

This small book is intended to serve as a practical guide for "bonificators" or sanitary inspectors in charge of anti-malaria measures in the state-managed (Collective and Soviet) farms. It provides the necessary elementary information regarding the bionomics of the mosquitoes, the methods of their destruction and the methods of protecting human dwellings from them. A brief account is also given of the treatment and prophylaxis of malaria. *C. A. Hoare.*

LOGIE (H. B.) [M.D., C.M., Executive Secretary]. [Edited by.] **Standard Classified Nomenclature of Disease. Compiled by the National Conference on Nomenclature of Disease.** [2nd Edition.]—pp. xxi+870. 1935. New York: The Commonwealth Fund. [15s.]

This book was first issued less than two years ago; the second edition contains 170 more pages than the first, but the book is not materially increased in size and the price has been reduced. The preface affirms that the work has been well taken up in America and has found its way into nearly 500 hospitals in the United States and Canada. By retaining communication with those working at these hospitals the authors have been able to avail themselves of the experience gained and use it in preparing the present edition. The same general plan has been followed, but changes have had to be introduced in all sections and two have had to be re-written. It attempts to include any morbid condition clinically recognizable.

The work must have entailed a vast amount of labour and only time and experience can tell whether the results will be commensurate. Many will not be inclined to agree that it will prove labour-saving, as the reviewer's experience may demonstrate. The user is directed to "read the introduction and consult the index" before setting out to designate the disease by numbers. Probably considerable practice and more thorough knowledge of the rules of the game are needed. Following directions, the reviewer looked out Sprue, and found it given in the index as 113 (7). The number in brackets we are told "refers to the etiological category" *i.e.*, metabolism, growth or nutrition. So far so good. Page 113 gives "sprue" and against it 010-703. Now 010 appears (p. 106) to stand for "Body generally" (somewhat arbitrarily, perhaps). To track down 703 we turn to the "etiological category" and find on p. 82, that 70 is "disturbance of general nutrition" and 703 "deprivation of a particular kind of food." How far this is a true interpretation of sprue is a matter of opinion which will vary according to the views of the physician treating the patient. After trying to trace other tropical conditions we found the game quite absorbing and more than once had to leave the problem unsolved feeling that as a winter evening's employment it is every bit as intriguing and perhaps as instructive as the average crossword puzzle. We were, however, convinced that it would be quickly and more readily comprehended to enter the diagnosis as Sprue (*tout court*) and place the

card in the S. section. As was stated in the review of the first edition [see this *Bulletin*, Vol. 30, p. 329]: "In this country [Great Britain], however, and throughout the British Empire, the Nomenclature of Diseases [Royal College of Physicians] must continue to form the basis of all official records for the present," and until the methods of this work under review are much simplified we feel that it is better so.

H. H. S.

MAJUMDAR (Akhil Ranjan) [M.B., Bengal Medical Service, etc.]. **Bed-Side Medicine. A Hand-Book of Medical Diagnosis, Symptoms, Physical Signs and Laboratory Methods, from Tropical Standpoint.** Third Edition.—pp. xii + 815. With 248 figs. 1934. Calcutta: The Book Company, Ltd. 4/4a College Square. [8 rupees.]

A book that has reached a third edition within about six years of the publication of the first has surely proved its utility and popularity. Dr. A. R. Majumdar's "Bedside Medicine" differs from the usual book on clinical diagnosis by the larger amount of space given to tropical diseases, and it is a great advantage to see the symptoms of these set out side by side with those of the diseases of cosmopolitan distribution.

The book has been considerably enlarged since the second edition was reviewed in this *Bulletin* (1931, Vol. 28, p. 336), and new diagrams and illustrations have been added, but it still remains of a convenient size.

After describing the procedure for the routine examination of a patient—with, incidentally, a sound caution against the temptations of a "lightning diagnosis"—the author contrasts the different kinds of fevers, and then goes on to a detailed account of the derangements of the various systems of the body. All these sections are very complete; that on the nervous system is particularly lucid. Wherever the book has been tested, it has been found to be reliable and up to date in its information. It does not replace a good textbook, and it is not meant to do so; but it will be a very useful aid to revision for students and practitioners. Quite apart from the large number of important facts of which he will be reminded, the student, who reads the book carefully and takes its method to heart, will have gone a long way towards the acquisition of an orderly mind, and will have learned to approach the very important subject of diagnosis in the only satisfactory way, which allows of no short cuts.

There are about 250 illustrations, most of which are quite adequate; the book is strongly bound, and well printed in type of a reasonable size, and the price (eight rupees) is extremely moderate.

H. J. Walton.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 7.]

PELLAGRA.

CORKILL (N. L.). **Pellagra in Sudanese Millet-Eaters.**—*Lancet*. 1934.

June 30. pp. 1387-1390. [11 refs.]

——. **Pellagra in the Sudan.**—*Jl. Trop. Med. & Hyg.* 1934. June 15.

July 2, July 16, Aug. 1, Aug. 15 & Sept. 1. Vol. 37. Nos. 12, 13, 14, 15, 16 & 17. pp. 177-183. With 1 map; 196-204. With 2 graphs; 214-218; 231-236 [34 refs.]; 245-251; 265-270.

These two papers, considered together for convenience sake, deal with an outbreak of pellagra among a tribe of Arab millet-eaters in the Sudan.

The rarity of pellagra in the Sudan has been ascribed to the fact that the Sudanese are mainly millet-eaters, whereas in Egypt, where the disease is common, maize is largely consumed. WILSON, however, has recorded pellagra in Egyptian millet-eaters.

The present papers deal with the author's clinical findings and conclusions based upon investigations carried out in a community of Arabs at Abu Deleig in the Butana Desert of the northern Anglo-Egyptian Sudan. Some 16 females and 33 males were found to be in an active stage of the disease. In the period of maximum incidence of the malady (hot, dry season) the vitamin supply, *i.e.*, milk, sinks to a level of practical deprivation. Millet alone remains as a food item and the biological protein value of the diet during this season is then below Wilson's critical value of 45 grams. At this time, too, there is marked deprivation not only of vitamins A, C and D, but also of the food sterols.

It is suggested that "three or more of certain physical signs, namely deepened pigmentation of the cheeks and forehead, the sulphur-flaking appearance on the nose, cheeks and forehead, blue or black gums, blue or black patches or points on the tongue and the impression of the teeth on the buccal mucosa justify a diagnosis of pellagra in the Sudan." The disease has three stages or phases: (1) in which the signs just mentioned are present, but subjective symptoms are absent. (2) in which physical signs are more pronounced and symptoms supervene; and (3) in which physical signs are less obvious and symptoms absent or only present after exposure or fatigue. The first and

third stages are regarded as latent pellagra. It is to be noted that objective signs of typical dermatitis can rarely be appreciated in pigmented Sudanese. Such factors as sex, age, occupation, katabolic acceleration (fatigue, disease and snake poison), insolation, season and diet affect the course and nature of the disease. Dental caries and pyorrhoea were commonly found, but it was observed that the severer the pellagra the less was the degree of caries. Of the 16 female pellagrins, 9 were melancholics and of the 33 males 4 presented some mental change. Suicide seems to have been relatively frequent in this community.

The author is of the opinion that "pellagra is essentially an allergic disease and that deficiencies of the vitamins A and C contribute their characteristic effects to the syndrome as do also cereal toxamins. Further, it is suggested that the body's cholesterol is mobilized for photosynthesis of vitamin D in the skin and that withdrawal of cholesterol from the central nervous system, the gonads and adrenal cortices, is responsible for some of the manifestations of pellagra." The characteristic dermatitis is an allergic response to sun trauma and pigmentation is protective. The sebaceous dysfunction (sulphur-flaking) so commonly met with in pellagra indicates a heavy photosynthesis of vitamin D and it is suggested that this vitamin, and not vitamin B₂ (the existence of which is doubtful) is the true anti-dermatitis factor.

The disease in the Sudan should be controlled by increasing the cultivation of vitamin- and phytosterol-yielding crops.

[These two papers record a very large amount of work and so numerous are the observations made that it is difficult to do them full justice in a short abstract. Only some of the author's observations and conclusions can be mentioned.]

A. D. Bigland.

YANG (Chi-Shih) & HUANG (K. K.). **An Outbreak of Pellagra in Nanking. A Report of 30 Cases.**—*Chinese Med. Jl.* 1934. Aug. Vol. 48. No. 8. pp. 701–723. With 1 fig. [76 refs.]

An outbreak of pellagra among soldiers in Nanking is described, together with full details of 30 cases.

In 1920 the first report of pellagra in China was made, 4 cases being observed by JOUVEAU-DUBREUIL in Szechuan [see this *Bulletin*, Vol. 15, p. 283]. Since then small groups of cases have been reported from time to time, but the present paper deals with the first epidemic recorded in China. Thirty typical cases of the disease occurring in soldiers belonging to two camps in Nanking are described. The usual skin manifestations were present and out of 27 cases examined by sigmoidoscope 11 showed inflammation or ulceration of the rectum and lower colon. Of the 30 cases, 27 suffered from inflammation of the tongue and oral mucous membrane. With reference to the presence of glossitis, the following statement is of interest: "In the cavalry camp of 148 inmates among whom 29 cases of pellagra have been observed, 80 soldiers have variable degrees of this condition, while in the artillery group of 128 men with three cases of pellagra, over 70 showed definite signs of glossitis." Achlorhydria was found in only 3 out of 21 cases examined. Varying degrees of night blindness were recorded in 19 of 25 cases examined; there was one case of retro-bulbar neuritis and one of keratomalacia. The blood findings revealed no special points of

interest, and the same may be said of neurological investigations with the exception that the patients were all normal mentally.

As regards diet it was found that these soldiers had been living upon a ration containing less than 10 gm. of animal protein a day. Nevertheless, the same diet was consumed in other camps where no pellagra was found. For purposes of treatment, cases were divided into two groups: (1) In addition to the ordinary hospital diet, these patients were given a daily ration of 30–50 gm. of animal protein. (2) This group received 100–120 gm. of protein. Yeast in 3 gm. daily doses was given to all. No results warranting generalization were obtained, but it is recorded that no deaths occurred.

The authors draw attention to the multiple deficiency conditions present in some of these cases and they are of the opinion that "pellagra is a symptom complex rather than a disease entity due to the deprivation of one single food factor." A. D. B.

YU (K. Y.). **Pellagra in Manchuria. Report of Three Cases.**—*Chinese Med. Jl.* 1934. Aug. Vol. 48. No. 8. pp. 724–735. With 6 figs. on 2 plates. [26 refs.]

An account is given of three cases of pellagra in Manchuria. This is the first record of the disease in this country.

Pellagra has never before been recorded in Manchuria. The three cases were all of the female sex, in which the disease was associated with other conditions, viz.: chronic amoebic dysentery, ankylostomiasis and tuberculosis. In all a monotonous and inadequate diet had been taken. The first two cases responded well to treatment (diet, yeast, thiosulphate, hydrochloric acid, etc.) but the last case, on account of tuberculosis, did not improve. Among the investigations made the following may be noted: oedema over the front of the legs, with high chloride and low total protein contents of the blood, was present in all; so also was indicanuria. Hypochlorhydria was found in two cases and achlorhydria in one. Blood calcium findings were normal in the first case, in the second case the figure of 14.6 mgm. per 100 cc. of serum was obtained; in the third case hypocalcaemia (8.2 mgm. per cent.) was present. In two cases examined haematoporphyrinuria was not detected and the diastatic index of the urine was normal. Clinically the cases presented typical appearances. A. D. B.

MILLS (Stephen R.). **Alcoholism and Pellagra.**—*U.S. Nav. Med. Bull.* 1934. Oct. Vol. 32. No. 4. pp. 493–497. With 1 plate.

Discusses a series of pellagra cases in which a common etiological factor was alcoholism with consequent deficient food intake.

Twelve cases of pellagra were admitted to the Naval Hospital, League Island, Pa., during the summer of 1930. The disease is relatively uncommon in this district. Three cases are described in detail and all presented the following features:—alcoholism, glossitis and angina, achlorhydria, enterocolitis and colitis, dermatitis, delirium or dementia, and emaciation; four cases ended fatally.

In most of the cases symptoms of pellagra followed a prolonged alcoholic debauch with consequent marked limitation of food.

A. D. B.

URBACH (Josef). Sporadische Pellagra in Wien und Niederösterreich. [**Sporadic Pellagra in Vienna and Lower Austria.**—*Med. Klin.* 1935. Jan. 18. Vol. 31. No. 3. pp. 79–82. With 1 fig.

Five cases of sporadic pellagra occurring in Austria are described.

Of the five patients, four lived in Vienna and one in lower Austria. There were four women and one man, their ages being about 60. Two cases may be described as primary, while in three, pellagra was associated with gastric carcinoma, chronic phthisis and chronic epilepsy respectively. A one-sided deficient diet was the probable cause of the disease, but in two patients alcoholism was a marked feature. None of the sufferers had lived upon maize, but all had had a protein-deficient diet. Three recovered without any special treatment and the two deaths were due to the primary cause to which pellagra was only secondary.

A. D. B.

SPIES (Tom D.), PAYNE (Warren) & CHINN (Austin B.). **A Note on the Relationship of Pellagra to Pernicious Anemia.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Nov. Vol. 32. No. 2. pp. 328–330. [10 refs.]

In some respects pernicious anaemia and pellagra may be regarded as similar conditions. The present paper gives the result of yeast treatment in both diseases. Failure is recorded in the former and success in the latter.

Pellagra and pernicious anaemia are both special types of deficiency disease and they have in common, achylia gastrica, glossitis, peripheral neuritis and central nervous system changes. Spies and Payne have shown that the gastric secretions of pellagrins contain the necessary "intrinsic factor," since remissions in two patients with pernicious anaemia were obtained by the injection of a mixture of beef muscle and achylic gastric juice derived from acute pellagrins. These authors suggest that pellagra results from inadequate food ingestion, whereas pernicious anaemia is caused by the failure of the gastric juice to manufacture an anti-anaemic substance from food. STRAUSS and CASTLE have found that the "extrinsic factor" in food is associated with vitamin G.

In view of the fact that in certain cases of pellagra and pernicious anaemia a cure has been obtained by the administration of yeast, the authors of the present paper have studied the therapeutic effect of autoclaved brewer's yeast in the two diseases. For this purpose five typical cases of pernicious anaemia, and 30 cases of typical pellagra were selected. In the pernicious anaemia group, after 10 daily injections of a mixture of 150 cc. of normal gastric juice and 50 gm. of yeast no change in the blood picture was noted. Each of these pernicious anaemia cases, however, responded at once to liver extract administered intramuscularly. On the other hand, the pellagrins were given a diet deficient in pellagra-preventive substance together with a daily dose of 50–100 gm. of yeast. All signs and symptoms promptly disappeared.

"The present study suggests that the chemical substance in yeast utilised by the pellagrin to remit his disease, is not the same as the precursor of the anti-anaemic factor found in food (extrinsic factor)."

A. D. B.

SLATINEANU (A.) & BALTEANU (J.) in Collaboration with M. SIBI, J. NITZULESCU, M. FRANCHE, L. CANTACUZINO, Z. PARASCHIVESCU, E. VEIT & D. LUPU. Contribution à l'étude des troubles métaboliques dans la pellagre. Exploration fonctionnelle du foie et du rein. [**Metabolic Derangements in Pellagra.**]—*Arch. Roumaines Path. Expér. et Microbiol.* Paris. 1934. Sept. Vol. 7. No. 3. pp. 365–391. [54 refs.]

Certain biochemical investigations carried out upon 70 pellagrins in Rumania are here recorded.

All the cases were examined during the stage of erythema. The following findings are presented. (1) The various functions of the liver were investigated (ammoniogenetic, glycogen regulation, pigmentary and chromogogic). It was found that 88 per cent. of cases showed more or less characteristic alterations in at least one of these functions. Out of 62 patients signs of hepatic insufficiency were noted in 55. (2) Kidney functions were investigated in respect of Ambard's constant, phenolsulphonaphthalein elimination and the power to concentrate sodium chloride. Ambard's constant was defective in 25 cases, elimination of P.S.P. was insufficient in 17 cases, and there was a poor concentration of sodium chloride in 13 cases. Nineteen cases gave normal figures. (3) As a result of hepatic insufficiency, and often of renal insufficiency also, it was found that a large percentage of cases showed acidosis revealed either by raised ammoniacal coefficients, or diminution of alkaline reserve, or sometimes by the pH of the blood and urine. The authors are of the opinion that in certain cases such hepatic and renal insufficiency, associated with acidosis, may explain some of the metabolic disturbances met with in pellagra and may also perhaps account for some of the symptoms of the disease. A. D. B.

CRANE-LILLIE (Margaret) & RHOADS (C. P.). **Pathology of the Central Nervous System in Canine Black Tongue.**—*Arch. Pathology.* 1934. Oct. Vol. 18. No. 4. pp. 459–472. With 5 figs. [18 refs.]

So many similarities between pellagra and canine black tongue have been recorded that many observers regard the two diseases as one and the same. The characteristic nervous system changes in pellagra, however, have not as yet been found in black tongue. The present paper deals with this discrepancy and it is reported that neuropathological changes in fact do occur in black tongue.

Canine black tongue and pellagra both present similar symptoms, e.g., stomatitis, glossitis, salivation and diarrhoea. In fact WHEELER regards the two diseases as one and the same, "on account of their seasonal and geographical incidence, their common cause and similar course, their identical pathological changes and their equal response to the same therapeutic and preventive measures." One great pathological difference, however, has been recorded; in pellagra there are characteristic changes in the central nervous system, while in black tongue these are said to be absent. "This discrepancy is of more importance because of recent studies showing the effect of lack of the vitamin B complex on the production of lesions of the central nervous system marked by loss of myelin." Such degenerative lesions of myelin and nerve cells are undoubtedly present in pellagra and the authors here consider the possibility that similar changes in canine black tongue have been overlooked by previous workers. Accordingly

the brains and spinal cords of 12 dogs dying of acute black tongue were examined by modern neuropathological methods. In all the animals slight disintegration of myelin was found together with irregularity, swelling and shrinking of the fibres, but only occasionally was the myelin actually broken down into droplets. Alterations in the axones and degenerative changes in the nerve cells were also recorded. In short, "the changes observed were similar in many respects to those seen in pellagra. These changes were also similar to those described as occurring in animals kept on diets deficient in vitamin B complex."

A. D. B.

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- BRESTER (A.) & HULST (L. A.). Een geval van vermoedelijk secundaire pellagra. —*Nederl. Tijdschr. v. Geneesk.* 1935. Jan. 12. Vol. 79. No. 2. pp. 158-166. With 1 plate. [23 refs.] English summary (8 lines).
- CAVALCANTI (L. Robalinho). Pellagra. Considerações sobre tres casos de erythema pellagroide.—*Brasil-Médico.* 1934. Dec. 8. Vol. 48. No. 49. pp. 1017-1028. With 3 figs. [39 refs.] English summary.
- FLINKER (Robert). Pellagra und Pellagroid. Eine prinzipielle Feststellung.—*Schweiz. Med. Woch.* 1935. Feb. 9. Vol. 65. No. 6. pp. 137-138.
- MEYER (Fr.). Zur Klinik der Pellagra.—*Klin. Woch.* 1934. Sept. 29. Vol. 13. No. 39. 1401-1402.
- O'FLYNN (J. A.). A Case of Pellagra.—*Jl. Roy. Nav. Med. Serv.* 1935. Jan. Vol. 21. No. 1. pp. 54-57. With 1 fig.
- SLOT (J. A.). Een geval van pellagra, waarschijnlijk als gevolg van een chronische darmziekte.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Jan. 22. Vol. 75. No. 2. pp. 124-130. With 2 charts, 1 text fig. & 3 figs. on 1 plate. English summary (6 lines).
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TROPICAL OPHTHALMOLOGY.

A REVIEW OF RECENT ARTICLES. XXIII.*

Conjunctiva.—FRANCOIS¹ has described a form of *catarrhal conjunctivitis* which he regards as being *due to the diphtheria bacillus* though membrane formation is absent. The disease is chiefly met with in newly-born infants and may be considered a form of ophthalmia neonatorum. A muco-purulent conjunctivitis is present and this is frequently associated with slight enlargement of the preauricular gland and a rhinitis. The trouble is refractory to ordinary treatment but is readily cured by antidiphtheritic serum. Corneal ulceration may complicate the conjunctivitis, but the disease is on the whole the most benign of all forms of diphtheritic conjunctival inflammation.

POWELL² has found that the inhabitants of a particular district in California are liable to attacks of *acute conjunctivitis* during hot and windy weather. This district was formerly a swamp, but reclamation has converted it into a very fertile land composed of peaty soil. Fires frequently involve large areas and the resultant fine ash mixed with silica particles and other salts is readily blown about. The attack occurs immediately after the patient has been struck by a sudden dust-laden gust of wind. A curious feature is that one eye only is attacked. The trouble is easily cured by ordinary simple measures.

HOARE³ has a useful suggestion to make regarding the fixation of *protective conjunctival flaps*. The premature retraction of these sliding flaps, owing to the friability of the membrane, is a fairly common experience; but if the bulbar conjunctiva is slightly undermined at the site of the proposed attachment and the free edge of the flap is implanted in the shallow pocket so formed (just as the apex of a pterygium is in a pterygium transplantation) some days will elapse before the flap recedes.

Trachoma.—MACCALLAN⁴ has made a survey of the incidence of trachoma in the British Empire. He remarks that the disease may escape notice in some parts owing to the attention of the Public Health authorities being directed to the study of lethal diseases and to the failure of medical officers who have no specialist knowledge to recognize its presence. He states "In the absence of fulminating epidemics of acute conjunctivitis superadded to trachomatous conjunctivitis a population may be universally infected with trachoma without any insistent demand for treatment or prophylaxis. For instance, in some parts of India trachoma runs an uncomplicated course, the affection being accepted as an ordinary or natural occurrence, while in Palestine

* For the twenty-second of this series see Vol. 31, pp. 858-862.

¹ FRANCOIS (J.). Catarrhal Diphtheritic Conjunctivitis.—*Brit. Jl. Ophthalm.* 1935. Jan. Vol. 19. No. 1. pp. 1-19. With 4 figs on 2 plates. [18 refs.]

² POWELL (Barton J.), Jr. Unilateral Conjunctivitis from Peat Dust.—*Amer. Jl. Ophthalm.* 1934. Mar. Vol. 17. No. 3. pp. 206-208.

³ HOARE (W. Wallis). Conjunctivoplasty. [Correspondence].—*Brit. Jl. Ophthalm.* 1935. Apr. Vol. 19. No. 4. pp. 235-236.

⁴ MACCALLAN (A. F.). Trachoma in the British Colonial Empire; its Relation to Blindness; the Existing Means of Relief; Means of Prophylaxis.—*Brit. Jl. Ophthalm.* 1934. Nov. Vol. 18. No. 11. pp. 625-645.

hideous epidemics more than decimate the eyes of the natives." School treatment constitutes the best form of prophylaxis and this is best carried out by a specialist, though instillation of drops made regularly by the schoolmaster may be valuable.

BUSACCA⁶ has published histological evidence in support of his view that Herbert's pits are due to focal thickenings of the corneal epithelium at points previously occupied by trachomatous nodules. Surface depressions tend to form during cicatrization of the nodules, but these depressions are at once occupied by proliferated epithelium. This results in the appearance of round greyish areas, which on superficial examination seem to be pits but are really filled by a transparent epithelium. Only exceptionally can a small depression be found at the centre.

MAJEWSKI⁶ has recorded his experience of trachoma among children in Cracow. Over a period of ten years he has cured 1,346 children and sent home a further 167 who were partly recovered but required further treatment. The chief interest in his paper lies in his recognition of the important part which scrofulous conditions play in the disease as he has found it. He states, too, that orphanages and asylums in Cracow are now practically free from the disease and that the bulk of his patients at this time come from the northern and eastern provinces of Poland. 667 days represented the average period of treatment. BUSACCA⁷ attributes the slight ptosis, which is such a characteristic sign in the early stages of trachoma, to the increased weight of the lid. In the later stages when the under-lying tissues in the upper fornix become involved disturbances occur in Muller's muscle and in the levator, and these may be sufficiently severe to cause a permanent ptosis.

TANG⁸ has reviewed our knowledge concerning the aetiology of trachoma and concludes that little progress has been made towards the solution of the problem. No advance is probable until a susceptible animal, other than man, is found. SHALOM⁹ recommends intra-corneal injection of cyanide of mercury in the treatment of severe trachomatous pannus. He employs a solution of 1 in 1,000 of a 2 per cent. novocaine in distilled water and claims that the injection is quite painless. "A few drops of the solution are injected slowly." The cornea assumes a greyish opaque colour during injection but clearing occurs in about ten or fifteen days. Recurrence may take place later but the injection can be repeated. It is necessary to employ a very fine needle.

⁶ BUSACCA (Archimede). On the Structure of Herbert's Pits.—*Brit. Jl. Ophthalm.* 1935. Jan. Vol. 19. No. 1. pp. 26–31. With 4 figs.

⁶ MAJEWSKI (Casimir). Sur l'activité thérapeutique de la station pour les enfants trachomateux de Witkowice (Pologne).—*Rev. Internat. du Trachome.* 1934. Oct. Vol. 11. No. 4. pp. 198–203.

⁷ BUSACCA (Archimede). Ptsi transitorie e ptsi permanenti nel tracoma.—*Rev. Internat. du Trachome.* 1934. Oct. Vol. 11. No. 4. pp. 204–214. With 2 figs. French summary.

⁸ TANG (F. F.). Recent Progress in the Study of the Etiology of Trachoma.—*Chinese Med. Jl.* 1934. Sept. Vol. 48. No. 9. pp. 839–846. [21 refs.]

⁹ SHALOM (Elias S.). Intra-Corneal Injections of Cyanide of Mercury in Trachomatous Pannus.—*Brit. Jl. Ophthalm.* 1935. Feb. Vol. 19. No. 2. pp. 107–111.

Ginger is another novel remedy which has been recommended by SOLOTNITZKY.¹⁰ One part of powdered ginger is mixed with three parts of powdered sugar candy and the mixture strained through a silk sieve. The powder is applied to the everted lids and the eyes are closed for five minutes. During this time considerable pain may be experienced. The lids are again everted and the conjunctival sacs thoroughly irrigated in order to remove every particle of the remedy. A curious feature is that at first the patients tend to fall asleep for four or five hours after the application. The treatment is claimed to be specially useful in cases complicated by pannus and corneal ulceration. MOURZINN and SOUCHKOWA¹¹ have found that the lysozyme content of the tears is lower in trachoma than in other diseases of the eyes. TALBOT¹² as the result of his experience in Southern Tunis considers that prophylactic measures which fail to combat infantile infections are useless. The disease seen in the adult is merely a recrudescence of a latent infection contracted during infancy. Infection during school age is exceptional and trachomatous school-children have been infected in their homes. ALVARO¹³ suggests that the low incidence of pterygium amongst trachomatous patients which is claimed by some writers may be due to the photophobia which causes them to keep their eyelids semi-closed and thus to protect the bulbar conjunctiva from sources of irritation likely to cause pterygium.

STAHOVSKY¹⁴ has had good results from the use of subcutaneous injections of yatren in trachoma, and has recorded six cases which seem to have derived undoubted benefit from the injections.

Cornea.—*Keratomalacia.*—Gow¹⁵ has found that 2.9 per cent. of the eye patients attending the Mukden Hospital suffered from keratomalacia. The disease was most prevalent during the month of April, and infants, children and adults were attacked. The usual treatment of cod liver oil gave good results.

Leukoma.—KIRWAN¹⁶ has reported two successful cases of *corneal grafting* in opaque cornea. Both patients had suffered from interstitial keratitis and the opacity was sufficient to render them completely blind in the affected eye. Pre-operative treatment is important, both local and constitutional. A 4 mm. trephine is used for the donor eye and a 5 mm. trephine for the recipient. Both eyes are kept bandaged for a week and the affected one for a further fortnight.

¹⁰ SOLOTNITZKY (J. N.). Le traitement du trachome à l'aide du gingembre.—*Rev. Internat. du Trachome*. 1935. Jan. Vol. 12. No. 1. pp. 34-41. [10 refs.]

¹¹ MOURZINN (A. N.) & SOUCHKOWA (E. G.). Le lysozyme du liquide lacrymal dans le trachome.—*Rev. Internat. du Trachome*. 1935. Jan. Vol. 12. No. 1. pp. 1-15. With 3 diagrams. [14 refs.]

¹² TALBOT. La seule prophylaxie efficiente du trachome, fléau social.—*Rev. Internat. du Trachome*. 1935. Jan. Vol. 12. No. 1. pp. 15-24.

¹³ ALVARO (M. E.). Pterygion et trachome.—*Rev. Internat. du Trachome*. 1935. Jan. Vol. 12. No. 1. pp. 32-33.

¹⁴ STAHOVSKY. Ueber die Behandlung des Trachoms mit subkutanen Yatren-Injektionen.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Jan. Vol. 39. No. 1. pp. 28-30.

¹⁵ GOW (W. H.). Some Clinical Observations on Cases of Keratomalacia in Manchuria.—*Chinese Med. J.* 1934. Sept. Vol. 48. No. 9. pp. 885-889. With 2 figs.

¹⁶ KIRWAN (E. O'G.). Corneal Transplantation on Opaque Corneas.—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 61-62. With 3 coloured figs. on 1 plate.

Cataract.—PI¹⁷ found that only 0.66 per cent. of 12,111 patients of the Peiping Eye Hospital suffered from senile cataract. This small proportion may be due to three reasons; (1) Longevity is rare among the general population of China; (2) the people regard Western forms of treatment with suspicion; (3) an elderly person considers that inactivity is his rightful due and does not regard his disability seriously. The senile cataract age is five or ten years younger than in Germany or Japan. The same observer¹⁸ reports the occurrence of cataract in four patients suffering from osteomalacia. Osteomalacia is stated to be very prevalent in many parts of China.

PISCHEL¹⁹ reports a careful examination made by him of a series of unselected patients who had undergone operation for senile cataract at least two years previously. All had been operated upon at the Vienna clinic by MELLOR or by one of his assistants. In about half the number the lens had been extracted in its capsule, and in the remainder capsulotomy had been performed by removing the anterior layer of lens capsule with forceps. Only those intracapsular cases were considered which were entirely free from complication either at the time of operation or during convalescence; but no such selection was made in the case of the capsulotomy patients. The author furnishes an excellent review of the comparative advantages of the two forms of operation, and concludes that "while the results in the successful intracapsular operation are practically as good as those in the well-performed extracapsular operation, there are more bad results even in a selected series of intracapsular operations than in an unselected series of extracapsular operations." Only 6.9 per cent. of the capsulotomy patients required subsequent dissection, and this good result is attributed to the fact that a really large piece of the capsule is removed at the time of laceration.

Filariasis.—WRIGHT²⁰ has reported an intraocular infection by an adult *W. bancrofti*. The patient was a male Hindu, aged 25, resident in Madras and was admitted for an iridocyclitis of his right eye. Fine vitreous opacities, retinal haemorrhages and some optic neuritis were noted. Thirteen days after admission a filarial worm was seen moving rapidly about in the anterior chamber. The worm was removed three days later through a small keratome incision made in the cornea. In view of the difficulties experienced by Koman NAYAR in recovering the worm in a previous case, exceptional precautions such as surrounding the eye with a black mask and using a black dish to catch any fluid escaping from the eye were adopted. The worm escaped with the first drop of aqueous and, despite all precautions, was only found after a prolonged search with a binocular dissecting microscope. The patient made a good recovery; but his optic disc on discharge presented the appearance of a subsiding neuritis with commencing atrophy. The

¹⁷ PI (H. T.). Cataract among the Chinese.—*Chinese Med. Jl.* 1934. Vol. 48. No. 9. pp. 928-947. [40 refs.]

¹⁸ PI (H. T.). Subcapsular Cataract in Osteomalacia.—*Chinese Med. Jl.* 1934. Vol. 48. No. 9. pp. 948-964. With 9 figs. on 3 plates. [30 refs.]

¹⁹ PISCHEL (Dohrmann K.). Comparative End Results in the Intracapsular and Extracapsular Operations for the Removal of Senile Cataract.—*Amer. Jl. Ophthalm.* 1934. Apr. Vol. 17. No. 4. pp. 326-333. [29 refs.]

²⁰ WRIGHT (R. E.). Adult *Filaria* (*Wuchereria*) *Bancrofti* in the Anterior Chamber.—*Brit. Jl. Ophthalm.* 1934. Nov. Vol. 18. No. 11. pp. 646-650.

retinal arteries were narrow and thread-like and the peripapillary retina a dull grey colour. The haemorrhages had disappeared.

A similar case is reported from Ceylon by FERNANDO²¹. The patient was a Singhalese male, aged 26, who lived in a village ten miles from Colombo. The worm was visible in the anterior chamber and had given rise to some cyclitis. ARNDT removed it through a corneal incision. The worm emerged with the first flow of aqueous but was caught on the lips of the corneal wound and required to be removed with forceps. It was identified by W. FERNANDO as *W. bancrofti*.

Onchocerciasis.—WILSON²² reports an unusual case of onchocerciasis affecting the retina. The patient was a male aged 16 years. The uvea and anterior segment of the eye were perfectly normal. A short, greyish white thread-like object in constant wriggling movement could be seen attached by one extremity to the macula. The surrounding retina showed some mild inflammatory changes. The object was regarded as an *Onchocerca volvulus* owing to the circlets of protuberances which could be seen on the surface of the worm. The worm disappeared fifteen days later and its presence was followed by the development of an area of retinal atrophy. BRYANT²³ observed blindness to be extraordinarily rife amongst the population of the Bahr-el-Ghazal province. On investigation the bulk of the cases were found to be suffering from a gross form of retino-choroiditis associated with a secondary optic atrophy. Some blindness too, was due to typical onchocercal keratitis and the two conditions might be associated. The disease appears to have been introduced only recently and *Simulium damnosum* appears to have become more common also.

BOASE²⁴ when treating a patient for a syphilitic uveitis of his left eye found some signs of a past papillitis in the other eye. Owing to the occurrence of slight pain and lachrymation a slit-lamp examination was made and numerous small, white, thread-like bodies were observed wriggling through the aqueous. The author considers these to have been *Microfilaria perstans*. No sign of any uveitis was present in that eye whereas the other eye was free from filariae.

Cysticercus Cellulosae.—FENG²⁵ reports a case of subconjunctival cysticercus infection in a Chinese boy aged 13. The cyst was ovoid and measured 6 by 4 by 2 mm. It was painless and was situated near the insertion of the internal rectus muscle. Removal was easy. Although this is the first case reported from Peiping the author thinks the disease may not really be rare, and he urges greater care in diagnosis and in reporting cases.

²¹ FERNANDO (S. E.). Ocular Filariasis. (Adult *Wuchereria bancrofti* in the Anterior Chamber of Human Eye.)—*Jl. Trop. Med. & Hyg.* 1935. Jan. 15. Vol. 38. No. 2. pp. 17-18.

²² WILSON (Rowland P.). Onchocerciasis of the Macula.—*Eighth Ann. Rep. Giza Memorial Ophthalmic Laboratory, Cairo, 1933.* pp. 85-87. With 2 coloured plates.

²³ BRYANT (J.). Endemic Retino-Choroiditis in the Anglo-Egyptian Sudan and its Possible Relationship to *Onchocerca volvulus*.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 523-532. With 1 map & 5 figs. on 2 plates.

²⁴ BOASE (A. J.). Ocular Filariasis.—*East African Med. Jl.* 1935. Jan. Vol. 11. No. 10. pp. 326-328.

²⁵ FENG (H. H.). *Cysticercus Cellulosae* Subconjunctivalis. Report of a Case.—*Chinese Med. Jl.* 1934. Sept. Vol. 48. No. 9. pp. 863-868. With 3 figs. on 2 plates. [21 refs.]

Retrobulbar Neuritis.—CHEN P'AN²⁶ has recently observed an unusual number of Chinese patients in Nanking who suffered from retrobulbar neuritis. About 87 per cent. of the patients were soldiers and symptoms commenced from four months to four years after enlistment. Most were under thirty years of age. A central scotoma, relative or absolute, was the sole ocular sign. The cause is entirely obscure as in only very few could any of the ordinary factors be found. Treatment appeared to have no effect, but recovery seems to have taken place in course of time.

Eclampsia.—WRIGHT, NAYAR & NAYUDU²⁷ have investigated the visual changes amongst twenty-eight eclamptic patients in the Madras Government Hospital for Women and Children. Blindness without any demonstrable lesion is possible but very rare. Retinal haemorrhages and oedema without immediate interference with vision are relatively common. Retinal detachment following toxæmias of pregnancy is very rare.

Quinine Amblyopia.—A case has been reported by KING²⁸ in which a woman took about two teaspoonfuls of quinine [? sulphate] in order to procure abortion. Deafness, aphasia and partial blindness followed in three hours. The blindness increased during the next four days and vision was reduced to light perception whilst the pupils failed to react. The fundus at this time appeared normal with but little vessel change. Central vision began to return on the fifth day and a month later reached 6/9 partly, the visual fields being markedly restricted. There was then disc pallor with some vessel constriction. In discussing the case WOLFF suggested that the poison might reach the retina by way of the vitreous. This would account for the ganglion cells being affected before the vessels.

BERTRAND²⁹ in a survey of the most common diseases of the eye met with in North Togoland finds them to be in order, those of the posterior segment, of the lens, and of the cornea. The posterior segment diseases (choroiditis, retino-choroiditis, and optic atrophy) he regards as due to sleeping sickness. Senile cataract is on the whole comparatively rare and the lens troubles are mostly secondary to the above or to corneal inflammations. Corneal lesions are due to trauma or infection or both combined. The optic atrophy is of the primary type such as is often met with in syphilitic infections, but the author considers that the cause is undoubtedly sleeping sickness and that venereal disease may be excluded. No trachoma was seen in the country. Acute conjunctivitis is occasionally due to the Koch-Weeks bacillus, but more often occurs independently of any bacterial infection and is caused by the mechanical irritation of dust, etc. Gonorrhoeal ophthalmia when seen is rather benign in character and readily cured. [BRYANT'S

²⁶ P'AN (Chen). Retrobulbar Neuritis among the Chinese. A Preliminary Report.—*Chinese Med. Jl.* 1934. Sept. Vol. 48. No. 9. pp. 999–1005. [9 refs.]

²⁷ WRIGHT (R. E.), NAYAR (K. Koman) & NAYUDU (T. Vencatarangum). Disturbances of the Visual Apparatus in the Toxæmias of Pregnancy associated with Eclampsia or the Pre-Eclamptic State.—*Brit. Jl. Ophthalm.* 1935. Jan. Vol. 19. No. 1. pp. 19–26.

²⁸ KING (E. F.). Quinine Amblyopia.—*Proc. Roy. Soc. Med.* 1935. Feb. Vol. 28. No. 4. p. 354 (Sect. Ophthalm. p. 26).

²⁹ BERTRAND. Les maladies des yeux en pays cabrais (Nord Togo).—*Ann. de Méd. et de Pharm. Colon.* 1934. July–Aug.–Sept. Vol. 32. No. 3. pp. 338–349.

report on onchocercal blindness in the Sudan might be considered in connexion with this paper.]

In the Matthai lecture for 1934 WRIGHT³⁰ dealt with the chief preventible blinding diseases of childhood in Southern India. He considers that keratomalacia is almost certainly the principal one and crude codliver oil is the most efficient remedy. For prevention better conditions of life are essential. Trachoma seems to occur more commonly amongst Mahomedans than Hindus in India and is a disease of the unwashed. Here, too, prevention depends upon a betterment of hygienic and general conditions. Ophthalmia neonatorum plays a less important rôle in India than in the West, and the strain of the gonococcus met with may possibly be less virulent. Syphilis, though one of the chief causes of blindness in the adult plays a smaller part in the blindness of children. The number of persons blinded by interstitial keratitis is relatively small. Smallpox is responsible for a considerable amount of blindness, whilst the use of irritant remedies causes an incredible amount of mischief. Hereditary blinding diseases are extremely common and retinitis pigmentosa is the most important of them. Nothing but good could result from the sterilization of all those who are known to be potential transmitters of hereditary blinding diseases.

The Annual Report of the Giza Memorial Ophthalmic Laboratory for the year 1933³¹ is just as interesting as the previous seven. The Laboratory happily combines research, clinical work and teaching. Commenting on the incidence of various diseases, the Director, R. P. WILSON, remarks that ocular tuberculosis is remarkably rare in Egypt. The Koch-Weeks bacillus accounts for fifty-two per cent. of the purulent ophthalmias and the gonococcus for forty-eight per cent. The former infection is rife in spring and the latter in autumn. Between these two seasons bacterial growth is inhibited by the excessive temperature. The increased humidity of the autumn season favours the gonococcus which is unable to withstand the dryness of the early summer. Flies, too, are most prevalent in the early summer and in autumn and are less frequent in the height of the summer heat. Several interesting cases are reported, amongst them being one of probable onchocerciasis of the macula and another of schistosomiasis of the conjunctiva. Research in trachoma has been continued by E. H. STEWART who concluded that monkeys of the two genera *Papio* (baboons) and *Lasiopyga* (grivets) are completely susceptible to experimental infection with trachoma. He considers that Prowazek bodies are unlikely to be the cause of Egyptian trachoma. Filtrates of trachomatous matter are not infective, and the virus is not removed from the matter by repeated washings.

The Bulletin of the Ophthalmological Society of Egypt for the year 1934³², contains many interesting papers and case histories. SOLIMAN described his experiences during a visit to the various Continental Clinics and gave a full account of Sinclair's technique for the extraction of cataract. BARRADA reported in full the case of filarial invasion

³⁰ WRIGHT (R. E.). The Chief Preventable Diseases of Childhood.—*Jl. Madras Univ.* 1934. Dr. Elizabeth Matthai Lectures 1933-1934.

³¹ CAIRO. Eighth Annual Report of the Giza Memorial Ophthalmic Laboratory 1933 [WILSON (Rowland P.), Director].—168 pp. With numerous illustrations. 1934. [25 P.T.]

³² BULLETIN OF THE OPHTHALMOLOGICAL SOCIETY OF EGYPT. 1934. Vol. 27. Session 31. pp. xxxi+145. With numerous illustrations.

of the macula referred to above. DEMETRIADES reported three cases of optic neuritis which followed the administration of acetylarsan. Fortunately the trouble subsided without very serious damage to sight. BAKLY and BARRADA encountered a case of the very rare condition ophthalmomalacia. The patient was a girl, aged 23, and one eye was affected. This was soft. The cornea appeared nebulous owing to many wrinkles in Bowman's membrane. The anterior chamber was deep and the pupil contracted and inactive. There appeared to be a retinal exudate at the lower nasal side of the disc. The eye gradually recovered and she was discharged cured three months later. Relapse occurred, however, in two months time and recovery then was not so complete.

H. Kirkpatrick.

KALA AZAR.

FORKNER (Claude E.) & ZIA (Lily S.). **Further Studies on Kala-Azar. Leishmania in Nasal and Oral Secretions of Patients and the Bearing of this Finding on the Transmission of the Disease.**—*Jl. Experim. Med.* 1935. Feb. 1. Vol. 61. No. 2. pp. 183–203. [11 refs.]

In a previous paper (this *Bulletin*, Vol. 31, p. 656), the authors reported the discovery of leishmania in smears made from the nasal secretion, saliva and tonsil of cases of kala azar. It was further noted that the nasal secretion of 2 cases produced leishmania infection in hamsters. The present paper gives further details of these observations and experiments.

Up to the date of writing, the nasal secretions of 22 cases of kala azar have been examined with the result that leishmania have been discovered in 12, while smears from the tonsil of 10 cases have revealed parasites in three. In most of the cases prolonged and careful examination with due regard to the structure of the organisms has been necessary to discover them. The intraperitoneal injection of hamsters with the nasal secretion of 14 cases has shown that living parasites were present in 13. The similar injection of sputum or saliva frequently resulted in the death of the animals from sepsis, but in 8 cases this did not occur, with the result that later two were found to be infected with leishmania. Material from the tonsil of 2 cases produced infection in hamsters. The nasal discharge from 5 cases was injected on a single occasion into the nasal and oral cavities of hamsters. In one case only did infection occur. Repeated injections of this kind have been carried out in hamsters and in two human volunteers, but the experiments are not yet complete. Emulsion of material from an infected tonsil produced infection in the hamster when administered by the oral route. The general argument of the paper is in favour of the oral route of infection in kala azar by means of parasites which escape from subjects of the disease in the secretions. In tabular form are arranged the arguments for and against direct transmission from man to man and the conveyance of the disease through the agency of the sandfly, and the authors conclude that the evidence presented strongly supports a theory of transmission of kala azar by means of direct or indirect contact infection.

C. M. Wenyon.

BOGLIOLO (Luigi). Studi sulle leishmaniosi. VI. Sui rapporti tra sistema reticolo istiocitario e leishmanie. [**Relation between the Reticulo-Endothelial System and Leishmania.**]—*Pathologica.* 1934. Nov. 15. Vol. 26. No. 517. pp. 735–739. [29 refs.] English summary.

A study of cases of human and canine kala azar and oriental sore has led the author to the view that the parasitized cells are those of the reticulum of the haemolymphopoietic organs in the case of kala azar and those of the peripheral reticulum in the case of oriental sore. The cells from the two situations are indistinguishable and in both cases they have no bad effect on the parasites which, on the contrary, find in them a medium very favourable for their development.

C. M. W.

GIRAUD (P.). A propos de la transmission de la leishmaniose interne. Fréquence de l'atteinte par les tiques des jeunes enfants dans la région méditerranéenne. [**Transmission of K.A. in the Mediterranean Region, with Special Reference to Ticks.**—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 731-733.]

The author argues in favour of the view that infantile kala azar is transmitted by the dog tick in the Marseilles district.

Both infantile kala azar and "fièvre boutonneuse" occur in the district and both are found most commonly amongst young children. It is generally admitted that "fièvre boutonneuse" is conveyed by the dog tick, which attacks children more frequently and with much less irritation than is usually supposed. The author mentions a case of this disease in a child on which a search revealed an unsuspected tick fixed to the scalp and another case of the same disease which was followed by kala azar 2 months later.

C. M. W.

ANDERSON (Charles). Chronique du kala-azar en Tunisie. [**K.A. in Tunis.**—*Arch. Inst. Pasteur de Tunis.* 1934. Dec. Vol. 23. No. 4. pp. 455-464. With 1 map.]

From time to time is issued a list of the cases of kala azar which have been noted in Tunis by the Pasteur Institute. The last one appeared in September 1930, since when a number of new cases have come to light bringing the total to 123 cases diagnosed by spleen puncture since the identification of the first case in 1906.

A remarkable feature of the disease in Tunis is that of the 123 cases 80 were children of Italian parents. No reason can be offered for the apparent greater susceptibility of this particular race. Six of the cases were in adults (aged 16 to 38 years), the rest being in children (aged 5 months to 10 years). A map shows that the disease is distributed throughout the northern half of Tunis, one case, however, having been found at Tozeur in the extreme south where oriental sore is common.

Some interesting details of leishmania which have been maintained in culture in N.N.N. medium for a number of years are given. These comprise 6 strains from cases of human kala azar isolated from 1910 to 1929 and subjected to 122 to 608 subcultures; 2 strains from cases of canine kala azar isolated in 1911 and 1913 and subcultured 558 and 547 times; 4 strains from oriental sore isolated from 1909 to 1926 and subcultured from 179 to 597 times; 2 strains from the gecko isolated in 1917 and 1919 and subcultured 411 and 347 times; in addition mention is made of a culture of a trypanosome of the toad which was maintained for 8 years, during which it was subcultured 210 times.

C. M. W.

FRANCO (Enrico Emilio). Le leishmaniosi nelle Puglie. [**Leishmanial Infections in Apulia.**—Reprinted from *Boll. d. Accad. Pugliese di Sci.* 1934. Nov.-Dec. Vol. 10. No. 1-2. 46 pp. With 1 map. [62 refs.]

This is a general account of leishmaniasis as it has been found to occur in the Province of Apulia on the southern part of the Adriatic coast of Italy. In all there have been encountered 92 cases of kala azar and 4 cases of oriental sore. The general features of the diseases and the results of the investigations carried out, as far as they have gone, are similar to those which have been recorded for other parts of the Mediterranean region.

C. M. W.

COLARIZI (Arrigo). Osservazioni clinico-statistiche ed epidemiologiche sulla leishmaniosi in Roma. [**Leishmanial Infections in Rome.**]—*Policlínico*. Sez. Prat. 1935. Mar. 11. Vol. 42. No. 10. pp. 413-16, 419-20, 423-4, 427-9. With 1 map. [23 refs.]

The author reviews the situation as regards kala azar and oriental sore in Rome. From 1911 to 1934 there have been encountered in the city 25 cases of kala azar of which at least 6 were actual autochthonous cases. During the same period 3 cases of oriental sore were met with and of these 2 were autochthonous. Thus kala azar and oriental sore appear to be endemic in Rome. C. M. W.

SEI (Mo Ten). **Distribution of Kala-Azar in the Southern District of Manchoukuo. Part 4. Conclusion.**—*Jl. Oriental Med.* 1935. Feb. Vol. 22. No. 2. [In Japanese pp. 403-429. With 11 figs. on 4 plates & 1 folding map. [69 refs.] English summary pp. 35-36.]

From surveys carried out by the author it appears that kala azar is widespread throughout Manchoukuo. In the districts of Syusuishi, Fukuken and Yugakujo 200 cases were found. It occurs most commonly in children from 4 to 7 years of age. The natives are skilled in the diagnosis of spleen tumour in children, reference to which appears in old literature of China of about 600 A.D. This is perhaps the earliest mention of the disease. C. M. W.

PENNA (H. A.). [In Portuguese & English.] Leishmaniose visceral no Brasil. **Visceral Leishmaniasis in Brasil.**—*Brasil-Médico*. 1934. Nov. 17. Vol. 48. No. 46. In Portuguese pp. 949-950. In English pp. 950-953. With 3 figs. & 1 map.

MAYER (M.). Viscerale Leishmaniose in Brasilien. Nach Befunden von H. A. Penna.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 128-129. With 2 figs. (1 map).

The invention of the viscerotome, an instrument for puncturing the liver after death for the purpose of removing a piece of this organ for histological examination when autopsies are not possible, has opened up a number of new fields of enquiry. Designed primarily for the purpose of diagnosing yellow fever in cases which had died of a febrile disease of unknown origin, the instrument has thrown light upon the distribution of malaria, schistosomiasis and other infections in S. America, where a regular viscerotomy service has been instituted. During the 4 years preceding the end of September 1934, there were examined in this way some 47,000 human livers from patients who had died within 10 days of the onset of some febrile illness. An unexpected result has been the discovery in 41 cases of a hepatic leishmania infection, indicating the presence in Brazil of kala azar. The distribution of the infection is fairly general throughout the country, while the ages varied from 45 days to 56 years, 29 being under 10 and 25 under 5 years of age. Attention having been called to the infection, efforts are being made to discover cases clinically.

Commenting on these observations, the author of the second paper points out that MAZZA in 1926 reported 2 autochthonous cases of kala azar in children in Northern Argentine [this *Bulletin*, Vol. 24, p. 135], while BORSONE in 1928 recorded the case of a woman who had quartan

malaria and splenomegaly and at the same time cutaneous leishmaniasis. Leishmania were discovered in this case, not only in lymphatic glands, but also in the spleen by spleen puncture. The author wonders whether these cases with visceral leishmania infection are actually cases of kala azar or merely cases of the well known Brazilian leishmaniasis, in which the parasite has assumed a generalized distribution in the body.

C. M. W.

FRÓES (Heitor Prager). Leishmaniose visceral no Brasil e especialmente na Bahia. [**K.A. in Brazil.**]*—Brasil-Médico.* 1935. Jan. 26. Vol. 49. No. 4. pp. 109–112.

The recent discovery by PENNA of the existence of leishmania infection of the liver in a number of fatal cases of febrile disease in S. America has stimulated the author to write the article to call attention to the fact that the possibility of the existence in Brazil of kala azar has long been recognized, though in cases in which the disease was suspected laboratory confirmation by the discovery of the parasite has not been forthcoming.

C. M. W.

BOGOJAWLENSKI (N. A.), MELIKOWA (T. A.) & DEMIDOWA (A. J.). Die viszerale Leishmaniose bei Kindern des Kasach'schen Distrikts. [**K.A. in Children in Turkestan.**]*—Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 205–211. With 3 figs.

Kala azar is widely spread throughout Transcaucasia and in the present paper the authors give an account of the disease as it exists in the Kasach district of Turkestan, where it is common in children, amongst whom it exhibits the usual features of infantile kala azar. It occurs also in dogs, an examination of 137 of which gave a percentage of 19 infected.

C. M. W.

GIRAUD (Paul). Sur la lyse possible des *Leishmania* dans l'organisme après la mort. [**The Possible Lysis of Leishmania in the Body after Death.**]*—C. R. Soc. Biol.* 1934. Vol. 117. No. 36. pp. 1017–1018.

The author calls attention to the fact that sometimes it is not possible to discover leishmania in the organs after death though there is every reason to expect them to be present. The cause of this is not clear, for in certain cases it is easy to find leishmania in perfect condition when the organs are in an advanced stage of putrefaction. This disappearance after death has been noted by other observers and it is well to bear it in mind, for the *post mortem* failure to find leishmania may be no indication that the disease was not kala azar.

C. M. W.

ZIA (Lily S.) & FORKNER (Claude E.). **The Syndrome of Acute Agranulocytosis and its Occurrence as a Complication of Kala-Azar.***—Amer. Jl. Med. Sci.* 1934. Nov. Vol. 188. No. 5. pp. 624–639. With 10 figs. (2 on 1 plate).

From the study of cases of kala azar at Peiping Union Medical College, China, the authors have come to realize that an important complication of the disease is acute agranulocytosis similar to that

which may accompany angina or pyogenic infections. It is acute in onset, usually of short duration and terminates rapidly in death or recovery.

The first clinical manifestations of this syndrome in kala azar are weakness and a feeling of exhaustion coming on rather rapidly over a period of 12 to 72 hours. At this period there is an increasing leucopenia with a decrease in the number of granulocytes. The symptoms become more intense, the leucocytes frequently falling to from 500 to 2,000 per cm. with a complete absence or presence of very few neutrophils. After from 24 to 96 hours more alarming symptoms appear with high fever, redness and tenderness and ulceration of the mucous membranes. Unless there occurs spontaneously, or as the result of treatment, an increase in the number of neutrophils, the symptoms progress and the patient succumbs. The condition in some of the cases of kala azar has occurred at the end of a course of antimony treatment. It seems that apart from general and local measures which would suggest themselves the administration of derivatives of nucleic acid may be a life-saving procedure.

The paper gives details of the blood examinations and is illustrated by a number of charts showing the fluctuations in the number of granulocytes, monocytes and other cells of the blood. C. M. W.

ZIA (Lily S.) & FORKNER (Claude E.). **Acute Agranulocytosis of Kala-Azar : Negative Effect of Urea Stibamine and Neostibosan on Blood of Normal Rabbits.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Dec. Vol. 32. No. 3. pp. 536-538.

Owing to the fact noted in another paper that acute agranulocytosis may occur in kala azar during treatment with urea stibamine or neostibosan it was decided to observe the effect of the administration of relatively large doses of this drug on rabbits. One or other of these drugs was administered to a dozen animals but nothing comparable with acute agranulocytosis occurred. There was, however, hyperplasia of the spleen, lymph-nodes and bone marrow. Two of the animals showed cirrhosis of the liver and one proliferation of the bile capillaries. C. M. W.

FAN (P. L.) & SCOTT (Annie V.). **A Study of Noma complicating Kala Azar in Children.**—*Chinese Med. Jl.* 1934. Oct. Vol. 48. No. 10. pp. 1046-1057.

Amongst children suffering from kala azar in Tsinan, North China, noma is a serious complication, the general features and treatment of which in 33 cases is discussed in this paper.

Experience has shown that cases of noma derive great benefit from blood transfusion. The treatment with neostibosan consists in daily injections of the drug, the first dose being 0.1 gm., and the succeeding doses 0.2 gm. A total of 2 to 2.5 gm. is administered. A special diet is given, while the local lesion and the mouth are irrigated with a 1/2,000 solution of zinc chloride every one or two hours during the day, followed by the painting of the lesion with 2 per cent. mercurochrome solution. As a prophylactic measure against noma, every kala azar patient in whom the haemoglobin reading is below 50 per cent. is given a large blood transfusion before injections of neostibosan are instituted.

C. M. W.

PINEY (A.). **A Chapter of Accidents in a Case of Kala-Azar.**—*Lancet*. 1935. Apr. 6. pp. 809-810.

A case of kala azar in which during treatment with neostibosan the patient suffered from volvulus of the pelvic colon necessitating surgical interference, later from generalized oedema with suppression of urine relieved by injections of salyrgan and again a month later from a series of epileptiform fits followed by unconsciousness and return of the renal symptoms, which were again relieved by salyrgan. In spite of these set-backs a complete recovery ultimately ensued. C. M. W.

GIRAUD (Paul). Kala-azar très grave rapidement guéri par l'uréastibamine. [**Cases of K.A. treated with Urea Stibamine.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1935. Jan. 21. 51st Year. 3rd Ser. No. 1. pp. 39-40.

—. Kala-azar stibio-résistant, guérison après deux ans et demi de traitement.—*Ibid.* pp. 41-43.

The two cases described were instances of kala azar in young children in Marseilles. One case was very severe with a haemorrhagic syndrome. It responded at once to injections of urea stibamine, which was well tolerated. The other case was much more resistant to treatment. Courses of urea stibamine changed to neostibosan had to be interrupted owing to intolerance. Finally, improvement commenced when a course of radiotherapy over the spleen, combined with injections of acetylarsan and a course of short wave pyretotherapy had been given. After this three further courses of urea stibamine were successfully administered. C. M. W.

ANDERSON (Ch.). Nouveaux essais de culture de *Leishmania donovani*. [**Cultivation of *L. donovani*.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 130-133.

In a previous publication (this *Bulletin*, Vol. 30, p. 318) the author reported the successful culture of leishmania in media composed of milk. A further study of the subject has somewhat modified his earlier opinion and he now doubts whether a milk medium is likely to give any practical results from the point of view of the maintenance of cultures of these flagellates. The fact that a certain growth does take place suggests that the influence of milk may be worth investigation. C. M. W.

- i. NATTAN-LARRIER (L.) & GRIMARD-RICHARD (L.). Le développement des cultures de *Leishmania infantum* sur milieu N.N.N. "mouillé." [**Cultivation of *Leishmania* on Wetted N.N.N. Medium.**]—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 843-847.
- ii. PARROT (L.) & DONATIEN (A.). Sur la culture des *Leishmania* en milieu N.N.N. "mouillé."—*Ibid.* 1935. Jan. 9. Vol. 28. No. 1. pp. 39-40.

i. The authors make some further remarks (*ante*, p. 87) about the behaviour of cultures of leishmania in which the water of condensation of N.N.N. medium after a certain period of growth has been replaced by 2 cc. of physiological saline solution; if the tube is kept upright there is a delay in the multiplication of flagellates, whereas if it is

inclined, the growth is rapid. For the maintenance of cultures it is well to incubate in the inclined position for a few days after adding the saline solution and then to continue incubation in the upright position.

ii. The authors bear testimony to the value of this method and illustrate their remarks by quoting instances in which leishmania were kept growing for 58, 79 and 99 days respectively, saline having been added only once to each of the 3 tubes. C. M. W.

NATTAN-LARRIER (L.) & GRIMARD (L.). Les leishmanias peuvent-elles se multiplier par schizogonie? [**Can Leishmania multiply by Schizogony?**]*—C. R. Soc. Biol.* 1935. Vol. 118. No. 10. pp. 969-972.

On a number of occasions authors have described a process of multiplication of leishmania by schizogony, but most authorities have agreed that the appearances have been due to a mass of parasites being so closely packed together that in a dry smear the outlines of the individual parasites have ceased to be visible, so that the impression is given of a single cytoplasmic body containing a number of nuclei and kinetonuclei. Between these forms and masses of individualized parasites, it was easy to trace every gradation and to conclude that reproduction by schizogony was taking place. In the paper under review the authors describe appearances they have seen in preparations made from a Syrian hamster experimentally infected with canine kala azar.

While admitting that massing of parasites may occur as described above, they believe that true multinucleate forms are present and that they arise by growth and nuclear multiplication without immediate division of the cytoplasm. A number of such multinucleate forms are figured, some of them lying within vacuoles in endothelial cells. [It must be admitted that the figures show cytoplasmic bodies containing a number of nuclei and some, at any rate, of them may have arisen as the authors suggest. But, even if this be so, are the bodies schizonts in the strict meaning of the term and is the process true schizogony? In all the Trypanosomidae multinucleate forms occasionally occur during active multiplication, owing to delay in cytoplasmic division, but when division of such forms takes place, it is by repeated binary fissions and not by simultaneous budding of merozoites as in true schizogony, which is seen most characteristically amongst the Sporozoa].

C. M. W.

CHUNG (Huei-lan). **The Sedimentation Rate of the Blood of Patients with Kala-Azar.***—Chinese Med. Jl.* 1934. Nov. Vol. 48. No. 11. pp. 1101-1112. [19 refs.]

An investigation of the sedimentation rate both by the time and distance methods has shown that this was increased in all of 36 cases.

This was associated with a decrease in plasma albumin and an increase in globulin, euglobulin and fibrinogen. Even when correction for the anaemia which occurred in the cases was made, the rate was still uniformly above normal. The sedimentation time for the 36 cases

varied from 9 to 62 minutes. For 14 normal Chinese males the time varied from 270 to 3,960 minutes, *i.e.*, 4½ hours to 2¼ days.

C. M. W.

BRUMPT (E.) & GALLIARD (H.). Grande sensibilité du spermophile d'Europe, *Citillus citillus*, au virus du kala-azar chinois. [**Susceptibility of the European Spermophile to the Virus of Chinese K.A.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 1. pp. 21–23.

The case of kala azar of Chinese origin in a Frenchman (noted in another review) enabled the authors to prove that the European hamster (*Citillus citillus*) is as susceptible to the Chinese virus as CAMINOPETROS, ADLER and others have shown it to be to the European virus. Five hamsters inoculated intraperitoneally with rich culture died with heavy generalized infections after 45, 105, 125, 138 and 193 days respectively. A fatal infection was produced in a Palestine hamster (*Cricetulus auratus*), while 2 mice acquired a mild infection. In the hamsters the frequency of parasites in cells in the skin was a feature of the infections.

C. M. W.

NINNI (C.) & TRAMONTANO (V.). Transmission de la leishmaniose tropicale au cobaye. [**Transmission of Leishmania to the Guinea-pig.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1934. Sept. Vol. 6. No. 9. pp. 338–343.

By inoculating material from oriental sore directly into the lymphatic glands of guineapigs the author has infected this animal with *Leishmania tropica*. The parasites which were found in the gland up to about 40 days were also detected in histiocytes in the mucosa of the bronchi. The results indicate that the guineapig is not a very susceptible animal.

C. M. W.

PARROT (Louis). Évolution d'un hématozoaire du gecko (*Leishmania tarentolae*) chez un moucheron piqueur, du groupe des phlébotomes (*Phlebotomus minutus*). [**Development of *L. tarentolae* in *P. minutus*.**]—*C. R. Acad. Sci.* 1934. Nov. 12. Vol. 199. No. 20. pp. 1073–1074.

——. L'évolution de *Leishmania tarentolae* Wenyon chez *Phlebotomus minutus* Rond.—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 839–843. [10 refs.]

It has been known for some years that geckos (*Tarentola mauritanica*) in Algeria and Tunis are liable to a leishmania (*L. tarentolae*) infection, which can only be demonstrated by blood culture. It has been suggested by ADLER & THEODOR that a probable transmitter of this infection was *Phlebotomus minutus*, which was not present in Sicily where geckos were uninfected. The author describes experiments in which he shows that development of flagellates occurs in the stomach of this sandfly after feeding on an infected gecko. There is very active multiplication up to 48 hours after which the digested blood, together with the flagellates, passes into the hind gut to be completely expelled a day or two later. When this has occurred, flagellates can no longer be detected. It is supposed that geckos become infected by devouring sandflies harbouring these flagellates.

C. M. W.

ADLER (S.) & THEODOR (O.). **Investigations on Mediterranean Kala Azar. VII. Further Observations on Canine Visceral Leishmaniasis. VIII. Further Observations on Mediterranean Sandflies. IX. Feeding Experiments with *Phlebotomus perniciosus* and Other Species on Animals Infected with *Leishmania infantum*. X. A Note on *Trypanosoma platydactyli* and *Leishmania tarentolae*.**—*Proc. Roy. Soc. Ser. B.* 1935. Feb. 1. Vol. 116. No. 801. pp. 494–504. With 8 figs. on 2 plates; 505–515. With 2 figs.; 516–542; 543–544.

In these articles the authors continue the account of observations made during the investigation of Mediterranean kala azar in Malta and Catania (see this *Bulletin*, Vol. 29, p. 872).

VII On the subject of canine visceral leishmaniasis it is noted that heavily infected animals may appear to be quite healthy. Infection of the unbroken skin is present in all naturally infected animals and that this is not due to a cutaneous infection in the first place is proved by the fact that it occurs in dogs infected experimentally by intra-hepatic inoculation. Parasites occur in most of the organs and tissues of the body including the urethra, vagina, nasal and buccal mucosa, pharynx, tongue and intestine. The only factor common to all fatal infections was infiltration of the intestinal mucosa and submucosa with infected macrophages. It seems that the intestinal changes resulting from this infiltration are responsible for the emaciation which precedes death in fatal uncomplicated cases. Though infection of the eyes, mouth, nasal mucosa and urinary passages render possible escape of parasites from the body in the discharges this is of no importance for the spread of the disease. The infection rate in sandflies fed on infected dogs varies directly with the intensity of the skin infection and reaches almost 100 per cent. when the skin infection is heavy. A feature of the skin infection is that whether intense or not it is uniformly distributed over the body and involves, with other parts, the nose, internal surface of the ear and less hairy regions of the abdomen, places on which sandflies feed readily. Infected macrophages are found in all tissues except the central nervous system, ovary and testes. This applies not only to dogs but also to *Microtus*, *Citellus* and *Cricetus* experimentally infected.

VIII. Of the sandflies in Malta there are six species (*P. perniciosus*, *P. papatasi*, *P. parroti*, *P. major*, *P. sergenti* and *P. macedonicus*). The first named is by far the commonest but it has attracted less attention than the second owing to its relative infrequency in dwellings in the day-time. It is an out-of-door species and though it enters houses freely, far more specimens are to be caught outside where it feeds on dogs and human beings. In Malta it appears at the beginning of May and begins to disappear at the beginning of November. Hibernation of larvae actually starts in August in spite of a mean temperature of 27°C. to 28°C. at which development occurs earlier in the year. It becomes more marked between September and November, all development ceasing at a temperature of 20°C. Occasional sandflies are seen in December owing to the fact that a few larvae do not hibernate even at low temperatures. It is this sandfly, *P. perniciosus*, which is concerned with the spread of human and canine kala azar. Some further observations were made on sandflies in Catania, it being noted that the prevalence of *P. perniciosus* was underestimated in 1930

because it was not then realized that at suitable times it was more readily captured out-of-doors than within houses. A short visit to Greece revealed five species in Kavallah (*P. papatasi*, *P. sergenti*, *P. major*, *P. macedonicus* and *P. perniciosus* var. *tobbi*) and five species in Athens (the three first of the above series and *P. parroti* and *P. minulus*). In Athens *P. major* is the probable vector of kala azar. A new record for Palestine is *P. macedonicus*, a sandfly of the *major* group from the valley of Jezreel where a few cases of infantile kala azar have been noted.

IX. The feeding experiments described concern chiefly *P. perniciosus* but a number of other sandflies were also used. The sandflies were fed mostly on experimentally infected animals (Chinese and Syrian hamsters, spermophiles and dogs) but a number of experiments were also made by feeding on naturally infected children and dogs. Of the animals used, the spermophile is the most susceptible, a skin infection being established as early as 15 days after inoculation. The general result of the feeding experiments with *P. perniciosus* has shown that the distribution of the flagellates in the individuals of any batch of sandflies fed on an animal is subject to considerable variation, while there is a distinct difference in the behaviour of Maltese and Catanian strains of *Leishmania infantum*. The Maltese strain produces a large percentage of purely stomach infections during the greater part of the sandfly season, while the Catanian strain in most cases invades the anterior part of the cardia. In the case of the Maltese strain the infections in the sandflies become anterior towards the end of the sandfly season. Infections of the proboscis are rare with both strains but those that do occur are found mostly towards the end of the season and consist of short forms of the flagellate. From this it is inferred that infections of children occur in nature to a large extent at this season. This view receives support from the fact that at least half the cases in Catania are diagnosed from the end of April to the middle of July or six to eight months after the end of the sandfly season.

It was shown that inoculation into the skin of hamsters and spermophiles of flagellates removed by dissection from sandflies gave rise to infections. It was also demonstrated that heavily infected sandflies, if they had proboscis infections, passed flagellates into liquid in capillary tubes in which they were made to feed by the Hertig technique. In one case flagellates obtained in this way were inoculated intracutaneously to a spermophile which became infected. This was the nearest approach to the production of infection by the bite of a sandfly. It is recorded that of 150 *P. perniciosus* collected in a dog-house in Malta 4 were found naturally infected, a result which is not surprising in view of the fact that 11 per cent. of Maltese dogs are infected with *Leishmania infantum*.

A number of other feeding experiments were carried out showing that the infection rate in *P. major* is higher than in *P. perniciosus*. The latter sandfly, besides being infected by feeding on the animals, was also infected by feeding directly on cases of infantile kala azar. Other species of the *major* group (*P. major* var. *syriacus*, *P. perniciosus* var. *tobbi* and *P. chinensis* var.) were also infected from animals as also were *P. papatasi* and *P. sergenti* by feeding on very intensely infected animals. A number of sandflies (*P. perniciosus*, *P. perniciosus* var. *tobbi*, *P. major* var. *syriacus*, *P. chinensis* var. and *P. macedonicus*) were infected with an Indian strain of *L. donovani* by feeding them on inoculated hamsters.

X. An account is given of certain experiments with Maltese geckos infected with *Trypanosoma platydactyli* and *Leishmania tarentolae*. It was shown that the trypanosome infection in the geckos, which has usually been demonstrated by culture of the heart blood, can more readily be detected by feeding sandflies (*P. parroti* or *P. papatasi*) on them. An infection in the sandflies can be detected in three days. Of 43 *P. parroti* which fed on nine geckos infected with the trypanosome 40 became infected. The infection is an anterior one, flagellates occurring as far forwards as the oesophagus. No instance of hindgut infection was noted. One uninfected gecko appeared to have acquired a trypanosome infection by eating an infected sandfly which was being fed on it. Another gecko had both the trypanosome and leishmania infection, which in *P. parroti* produced a double infection of the two flagellates, both in the anterior position. C. M. W.

ROTTER (Werner) & CHAVARRÍA (Peña). Die Hautleishmaniose in Costa Rica. [Dermal Leishmaniasis in Costa Rica.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 89–99. With 12 figs.

The authors give an account of 50 cases of cutaneous leishmaniasis which they have seen in 4 years at the hospital at San José. This number of cases is an indication that the disease is fairly wide spread in the country.

The lesions assume various forms—ulcerating, non-ulcerating, nodular, verrucose—while a small percentage of the cases show lesions of the mucosae. The disease as regards severity appears to occupy a position intermediate between the oriental sore of the old world and the more serious muco-cutaneous condition met with in S. America. The paper is illustrated by a series of excellent photographs.

C. M. W.

WARMA (J. D.). Further Observations on the Treatment of Oriental Sore.—*Indian Med. Gaz.* 1934. Nov. Vol. 69. No. 11. pp. 616–620.

In a previous paper (this *Bulletin*, Vol. 29, p. 118) the author wrote of his experience in the treatment of oriental sore by local injection of berberine sulphate solution. With further experience he advocates the administration, in addition to the berberine sulphate treatment, of a vaccine prepared from cultures of the causative organism. This vaccine given at intervals of 4 to 7 days will itself bring about a cure of the sore in many cases, a feature which makes it very useful for the treatment of sores in places, such as the eyelid, where local interference is hardly possible. The maximum amount of berberine sulphate which can be injected at one sitting is about two-thirds of a grain or 4 cc. of a 1.0 per cent. solution. C. M. W.

SINCKE (G. E.). Zwei erfolgreich mit dem kombinierten Arsen-Antimonpräparat Sdt 386 B behandelte Fälle von Hautleishmaniose. [Two Cases of Dermal Leishmaniasis, treated with an Arsenic-Antimony Compound.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Feb. Vol. 39. No. 2. pp. 63–68. With 6 figs. [12 refs.]

In two cases of cutaneous leishmaniasis, one from Peru and the other from Baghdad, the author has obtained a cure by the intravenous use

of the arsenic-antimony compound mentioned in the title. Injections of 0.3 gm. of the drug were given every 4 or 5 days and were followed by rapid disappearance of acute inflammatory symptoms and gradual resolution of the sores, which was complete after 10 doses had been administered. The treatment did not give rise to unpleasant reactions.

C. M. W.

KRISHNAN (K. V.). **Factors concerned in the Causation of Dermal Leishmaniasis.**—*Calcutta Med. Jl.* 1934. Nov. Vol. 29. No. 5. pp. 205–214. [13 refs.]

It is well known that cases of kala azar in India which have apparently been cured by specific treatment may later develop a condition of dermal leishmaniasis. In some cases the skin condition is seen in individuals from kala azar districts who give no history of having had the disease. The disappearance of parasites from the internal organs as a result of treatment and their subsequent development in the skin is a phenomenon which has never properly been explained. The author discusses the problem from various points of view and reaches the conclusion that the immunity of the host has something to do with it, though he has not found it possible to explain precisely how this comes about.

C. M. W.

DE (Manindra Nath) & CHATTERJEE (Krishnadhan). **An Interesting Case of Dermal Leishmanoid.**—*Calcutta Med. Jl.* 1934. Nov. Vol. 29. No. 5. pp. 237–240. With 4 figs. on 2 plates.

A record of two cases of cutaneous leishmaniasis in brothers both of whom had suffered from and had been treated for kala azar 2 years before the appearance of the skin condition. The case of one of the brothers is described in some detail with illustrations which show how readily a diagnosis of nodular leprosy can be made, as was done in this case.

C. M. W.

MIHĂILESCU (M.) & NICOLOFF (D.). Două cazuri de leishmanioză spontană în România la câine. [**Two Cases of Canine K.A. in Rumania.**]—*Arhiva Vet.* 1934. Vol. 26. No. 1–2. pp. 43–53. With 7 figs. [13 refs.]

The paper describes two cases of canine kala azar from Rumania, presumably in Bucharest, where infantile kala azar was first noted by Professor MANICATIDE in 1912. Two figures illustrate elongate structures found in blood films. Though these are compared with herpetomonas, they bear no resemblance to this flagellate, so that neither they nor the two figures, which are presumably intended to show leishmania in spleen smears, help one to the conviction that the dogs were actually suffering from the disease diagnosed.

C. M. W.

AUGIER (Pierre) & FAURE-BRAC. La reviviscence transitoire des lésions cutanées au cours du traitement de la leishmaniose canine par l'antimoine. [**Lighting up of Skin Lesions in Treatment of Canine K.A. by Antimony.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 14. pp. 1432–1434.

It is well known that skin lesions of various kinds occur as complications of kala azar in dogs. The author has noted that about 8 to 10

days after the commencement of treatment with organic antimony compounds these skin lesions in a number of cases become temporarily aggravated and he compares the phenomenon with the Herxheimer reaction in human beings. C. M. W.

DONATIEN (A.) & LESTOQUARD (F.). Investigación de la leishmaniosis canina por las reacciones serológicas. [**Serological Reactions in Canine K.A.**].—*Medicina Paises Cálidos*. Madrid. 1934. Oct. Vol. 7. No. 10. pp. 486-487.

Writing of the serological reactions for the diagnosis of canine kala azar the authors point out that they consider the formol-gel test specific when gelification and opalescence occur within an hour. The turbidity produced by the addition of distilled water to the serum is also a valuable test. At the Pasteur Institute in Algiers for the past two years the two tests have been used simultaneously, not only for the diagnosis of canine kala azar but also for the purpose of controlling the treatment with organic compounds of antimony. C. M. W.

SINTON (J. A.) & SHORTT (H. E.). **Cutaneous Leishmaniasis as a Natural Infection of a Dog in India.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 393-396.

A dog born and bred at Kasauli, India, was taken for a few months to Karnal in the Punjab. After returning to Kasauli, there developed on its nose a number of small nodules which, on examination, revealed leishmania. It seems practically certain that infection was acquired at Karnal where human cases of oriental sore are seen from time to time and where sandflies of various species abound. C. M. W.

KOPACZEWSKI (W.). Gélification sérique et espèce animale. [**Gellification of Serum and Animal Species.**].—*C. R. Soc. Biol.* 1935. Vol. 118. No. 4. pp. 339-341.

The addition of acid to serum will produce a gelification on standing but the extent to which this occurs with any one acid is not the same for the sera of man, horse, ox and pig. Furthermore, the acid which gives the most marked reaction with the serum of one animal is not necessarily that which will give the most marked reaction with that of another. In general the degree of gelification is dependent upon the globulin content of the serum and the buffer action this has towards the acids. C. M. W.

THEODOR (Oskar). **Observations on the Hibernation of *Phlebotomus papatasi* (Dipt.).**—*Bull. Entom. Res.* 1934. Dec. Vol. 25. Pt. 4. pp. 459-472. [12 refs.]

The larva of *Phlebotomus papatasi* passes the winter in hibernation in Palestine. Is this due to the influence of external conditions, especially low temperature, or are there cyclical factors which cause hibernation to occur even when the external conditions would not do so?

As a preliminary to his studies the author standardized his methods of breeding and rearing, and describes a technique which nearly always gives consistent results. Much depends on preserving the necessary moisture in the food without allowing an excessive amount of water to be present. Using the methods described, the mean duration of the period from egg-laying to the emergence of the adult is 36-40 days at

30°C., and at least 75 per cent. of the eggs should produce flies. Under normal conditions it is the fourth larval stage which hibernates in Palestine, but if larvae in this state are disturbed, given food and put at 30°C., many of them will pupate though some cannot be re-activated.

In his experiments Theodor started with a culture which was isolated at the end of summer after four or five generations had been produced rapidly in nature. Some of the larvae developed without a pause, though the duration of larval life was a little longer than the normal, but others entered into a period of rest as large larvae, many of which pupated after an interval. Substantially the same results were obtained on several occasions during the winter. In the summer the proportion of larvae which rest is very much less, though the phenomenon is occasionally observed; and the duration of the larval stage is shorter than in the winter at the same temperature. The author concludes that hibernation depends principally upon climatic factors, of which it seems probable that temperature is the effective one, but there is some "cyclical" factor which operates in winter. Theodor's observations therefore support those of ROUBAUD, whose theoretical views about the "intoxication of the egg" and other matters remain in the realm of hypothesis.

P. A. Buxton.

SAINTE-MARIE (Flye). Un cas de leishmaniose viscérale infantile marocaine. Efficacité remarquable du traitement stibié. [Case of K.A. in a Moroccan Child.]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 183-187. With 1 chart.

The paper records a case of kala azar in a child 5 years of age from Zaouïa, Morocco. A visit to the locality did not reveal any other human cases but two dogs were found infected, one from the home of the child.

C. M. W.

MERKLEN (Pr.) & ISRAËL (L.). Un cas de kala-azar chinois; leishmanioses cutanées de formes variées. [Case of K.A. in a Chinese.]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Mar. 11. 51st Year. 3rd Ser. No. 8. pp. 352-358.

The case described is that of a man 33 years of age, who contracted kala azar during military service in North China. The diagnosis was made and the treatment carried out at Strasbourg.

C. M. W.

DECOURT (Jacques) & ARIÈS (Ch.). Sur un cas de kala-azar observé à Paris chez une adulte et rapidement guéri par la stibiothérapie. [Cases of K.A. seen in Paris.]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Feb. 25. 51st Year. 3rd Ser. No. 6. pp. 272-279. With 4 charts.

BENARD (René), POUMAILLOUX (M.) & BRINCOURT (J.). Un cas parisien de kala-azar traité par l'uréastibamine.—*Ibid.* pp. 262-272. With 3 figs.

FIESSINGER (Noël). A propos de la communication sur le kala-azar de René Bénard, M. Poumailloux et J. Brincourt.—*Ibid.* pp. 293-297.

These papers refer to two cases of kala azar in women, 17 and 42 years of age. Though the illness was in each case first noted in Paris, visits to the South of France render it probable that infection took place there.

C. M. W.

MACLEOD (J. M. H.). **The Lupoid Variety of Cutaneous Leishmaniasis.**—*Jl. Trop. Med. & Hyg.* 1934. Dec. 1. Vol. 37. No. 23. pp. 358–359.

The case described is that of an English woman who, during residence in India, developed a slightly raised, yellowish brown patch over the left malar bone. Owing to its resemblance to a tuberculous lesion, it was excised. Examined microscopically it did not show the characteristic structure of lupus, but revealed a leishmania infection. C. M. W.

GINANDES (George J.). **Kala-Azar in Children.**—*Amer. Jl. Dis. Children.* 1934. Dec. Vol. 48. No. 6. pp. 1336–1366. With 5 figs. [68 refs.]

The description of a case of kala azar in a Greek child, who had come to the United States 14 months before admission to hospital, together with reference to three previously reported cases in children from European endemic centres and some general remarks on the disease. C. M. W.

BOGLIOLO (Luigi). Studi sulle leishmaniosi. Prime ricerche ed osservazioni sui flebotomi della Sardegna *Phl. parroti* var. *sardous*, var. n. [**Leishmaniasis in Sardinia.**]—*Ann. d'Igiene.* 1935. Jan. Vol. 45. No. 1. pp. 41–47. With 9 figs. & 1 map.

The paper records the discovery in Sardinia of a sandfly which the author considers to be a new variety of *Phlebotomus parroti*. C. M. W.

D'OELSnitz, BONNET (G.) & RAYBAUT (A.). Observation d'un adolescent atteint de kala-azar et porteur de volumineuses adénites épitrochléennes. [**Case of K.A. in Adolescent with Large Epitrochlear Glands.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Jan. 28. 51st Year. 3rd Ser. No. 2. pp. 70–72.

The case described is of interest in that it is another instance of the occurrence of kala azar in adults in the South of France where the disease is now fairly common in children. Special attention is called to the enlargement of the epitrochlear lymphatic glands in this case, a feature which the authors have noted in other cases of the disease. C. M. W.

D'OELSnitz (M.), GALAVIELLE (R.) & RAYBAUT (A.). Kala-azar autochtone chez un jeune soldat. Stibio-résistance Guérison par un traitement stibié intensif.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Mar. 18. 51st Year. 3rd Ser. No. 9. pp. 428–432.

RATHERY (F.), DÉROT (M.) & CONTE (M.). Un cas de kala-azar chronique de l'adulte.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Mar. 4. 51st Year. 3rd Ser. No. 7. pp. 334–338.

HEAT STROKE.

MCMILLAN (J. S.). **Résumé of an Analysis of "Effects of Heat" Case Sheets for 1932.**—*Jl. Roy. Army Med. Corps.* 1934. Feb. Vol. 62. No. 2. pp. 129-132.

The author divides his 185 cases into four clinical groups. (1) Cases with no pyrexia. Ninety-one cases. Deaths nil. (2) Cases with moderate pyrexia throughout. Fifty-three cases. Deaths nil. Pyrexia ranged from 99.6°F. to 104°F. (3) Cases at first apyrexial which after a definite illness developed pyrexia. Sixteen cases. Nine deaths. (4) Cases with early hyperpyrexia. Twenty-five cases. Two deaths.

The importance of group 3 is stressed. In these cases, constant and distressing vomiting was a striking and almost constant feature during the apyrexial period, and the nervous symptoms exhibited at this stage were suggestive of further trouble to come. The patients were very dull, or very irritable and restless. Many were disrespectful or even insubordinate, and showed a mental attitude quite different from their normal. The length of time from the beginning of the attack until the onset of pyrexia was of help in arriving at a prognosis, for the longer the afebrile period lasted, the worse was the outlook. This group, as shown above, included most of the fatalities.

W. P. MacArthur.

SCHOFIELD (Richard O.). **Heat Prostration—its Treatment at Boulder Dam.**—*California & Western Med.* 1934. Aug. Vol. 41. No. 2. pp. 83-85.

An account of the body reactions to high temperatures in the presence of low humidity, as seen in California.

The summer of 1933 presented in Boulder City a daily average maximum temperature of 112°F. and a daily mean average temperature of 104°. Workmen were urged to drink large quantities of water, and to take in addition not less than one teaspoonful of salt daily. To this prophylactic measure is attributed in large degree the diminished incidence of heat exhaustion—in which term both thermic fever and heat syncope are included—as compared with the hot summer of 1931. In addition to continued application of warmth, or cold, according to the type of the attack, treatment consisted in giving normal saline in 7½ per cent. glucose intravenously, and normal saline subcutaneously. The results of treatment by saline injections are described as very satisfactory, and some of the speakers who took part in a discussion on the subject of the paper regarded this therapeutic measure as a specific.

W. P. M.

DREOSTI (A. O.). **The Prevention of Heat Stroke on the Mines of the Witwatersrand.**—*Proc. Transvaal Mine Med. Officers' Assoc.* 1934. Jan. & Feb. Vol. 13. Nos. 149 & 150. pp. 32-37. [32 refs.]

The author describes the classification of newly recruited native miners by the heat-chamber test, and their subsequent acclimatization.

The heat-chamber, which is a hospital annex, measures 50 feet by 25, and operates at a temperature of 98°F. in an atmosphere kept saturated by water atomizers, the conditions thus being more trying than those generally encountered underground. Each miner's temperature is recorded before he enters the chamber, after half-an-hour, and again at the conclusion of the test, which lasts for an hour. The experimental work consists in lashing rock from one to another of a series of troughs in the cement floor of the chamber, and the men are made to work at a rate at least as fast as that necessary in a mine. On completion of the test the men are graded as (a) Tolerant to heat, (b) Less tolerant, (c) Intolerant, in accordance with the degree of febrile reaction shown. These groups are then subjected to 4, 7 and 14 days' acclimatization, respectively, carried out below ground under the supervision of mine officials. After completing the allotted acclimatization period of reduced work, the men are issued with red armlets which are worn for a further period of from 7 to 14 days, according to grade. The badge indicates that the wearer is a recruit, and is not to be overworked in any way. At the end of the red-armlet period, the miner is considered acclimatized and is expected to do ordinary work.

During the two years that the heat-chamber has been in use, 10,000 men have been tested ; in all, only 8 cases of heat stroke have occurred, and none of these in the groups classified as heat-tolerant.

W. P. M.

BROWN (Earle G.). Deaths from Excessive Heat in Kansas, 1934.

—*Public Health Rep.* 1935. Apr. 19. Vol. 50. No. 16. pp. 546–548. With 1 fig.

The abnormally warm summer of 1934 was responsible for 291 deaths from excessive heat in the State of Kansas, this figure exceeding by about four times the highest previously recorded in the State. It is pointed out that the number of deaths from heat in 1934 was surpassed only by that due to motor car accidents and accidental falls in the group attributed to external violence.

The employment of a special report form supplemental to the death certificate provided the authorities with a considerable body of data regarding the fatal seizures. Two waves of mortality were recorded with the peaks occurring in July and August respectively, and in both months the bulk of the deaths followed on a number of days of exceptionally high temperature which varied between 106°F. and 110°F. It is interesting that throughout this period the relative humidity was abnormally low.

The proportion of the State population resident in towns of over 2,500 inhabitants is 30 per cent., and nearly half of the deaths were among town dwellers. The great majority of heat fatalities—249—occurred in persons at home, and only 27 were classed as industrial, of which agriculture gave 15. Of the 15 fatal seizures in public places, 4 occurred in persons driving in motor cars on the highway. As would be expected, the mortality fell most heavily on the older people and of the total deaths 73 per cent. were in persons of 65 years or over. But the young were not immune, and there were 14 deaths in infants aged less than one year.

W. P. M.

CHUN (J. W. H.). **An Analysis of 37 Heat Stroke Cases.**—*Reports National Quarantine Service.* Shanghai, China. 1934. Ser. 5. pp. 81–87. With 1 chart.

This paper records a series of 37 cases of heat stroke admitted to the Chinese Infectious Diseases Hospital, Shanghai, in 1934. The summer there, as elsewhere, was exceptionally hot, and for a period of 26 days the mean daily temperature was approximately 10°F. above the average, while the daily wet bulb temperature exceeded 80°F. During this time, the curve of the incidence of heat stroke cases closely followed the temperature curve. The commonest presenting symptom was hyperpyrexia, 27 per cent. of patients having a temperature of 107°F., and in one instance 109°F. was reached. Next in order of frequency came unconsciousness, cramp, diarrhoea, dyspnoea, and cyanosis. Over 35 per cent. of the cases ended fatally. The treatment followed recognized lines.

W. P. M.

CLIMATIC BUBO.

RAJAM (R. V.). **A Clinical Study of Climatic Bubo and Allied Conditions.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 546-554. With 3 figs.

A review of 183 cases of poradenitic infections coming under observation at the venereal clinic Madras General Hospital in the year 1933.

The distribution of cases was as follows:—

<i>Climatic Bubo.</i>					Males	Females
Climatic bubo only	99	2
Climatic bubo with other venereal diseases	51	1
with active syphilis	6		
with latent syphilis	6 (1 female)		
with positive strong Wassermann reaction in which there was no history or clinical evidence of syphilis	14		
with positive Wassermann reaction in which there was no history or clinical evidence of syphilis	10		
with gonorrhoea	5		
with gonorrhoea and active syphilis	2		
with chancroid	8		
with infective granuloma	1		
Genito-anorectal syndrome of the same aetiology	18	8
Elephantiasis vulva with or without ulceration	—	4
					168	15

Of the males 130 were Hindus, 13 Mohammedans, 3 Indian Christians, 3 Anglo-Indians, 1 European. The females were all Hindus. Among the cases of climatic bubo 120 were unilateral—right 64, left 56; bilateral 27. In 45 cases the iliac glands were also enlarged. Only one acutely toxic case was seen. Enlargement of the spleen never noticed. A certain number of cases showed a positive W.R. in the early stage in the absence of evidence of syphilis. Frei's test was found to show a high degree of specificity. It was positive in 21 cases exhibiting the "genito-ano-rectal" syndrome and in 4 cases of esthiomène. In 2 of the males suffering from the G.A.R. syndrome the test was negative. Many of the male cases appeared to have developed following the removal of poradenitic inguinal glands. This syndrome occurred in a total of 18 males, 16 to 55 years of age, and included 6 professional passive sodomists: in 8 females, 15 to 32 years of age, and included 5 prostitutes. The stricture of the rectum, discovered in many, had the characters which should now be well recognized.

Aspiration of softened glands combined with 6 injections of milk intramuscularly or dmelcos vaccine on alternate days followed by a course of foudadin to a total of 50-60 cc. of the solution has yielded the best results. Coexisting other venereal disease was not uncommon and must receive appropriate treatment. This paper forms a valuable contribution to the subject, the histories of the cases are good and the relationship of the poradenitis to other manifestations of this virus infection is well illustrated.

H. S. Stannus.

CHESTERMAN (Clément C.). Poradéno-lymphitis ou sixième maladie vénérienne au Congo Belge. [**Poradeno-Lymphitis or Sixth Venereal Disease in the Belgian Congo.**—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 413-420. With 2 figs. [Summary appears also in *Bulletin of Hygiene.*]

The author describes a number of cases of lymphogranuloma inguinale and of esthiomène in patients from the district between Stanleyville and Basoko (Belgian Congo) who were dealt with at the Baptist Mission at Yakusu. Such cases had been seen since 1920 but their true nature was not suspected until the author's attention had been directed to the possibility of their being L.I. by STANNUS's writings on the subject. The author mentions that he has also seen "the fourth venereal" disease caused by the organisms of Vincent's angina, but not the fifth or "granuloma venereum." He gives case notes of twelve cases proved to be L.I. by Frei's skin test, for which the antigen was made locally. Amongst the cases were six with some degree of stricture of the rectum. The author comments on the comparative intractability of the condition in women.

L. W. Harrison.

MASSIAS (C.). Maladie de Nicolas-Favre en Cochinchine. [**N.F. Disease in Cochín-China.**—*Bull. Soc. Path. Exot.* 1934. June 13. Vol. 27. No. 6. pp. 540-544. [11 refs.]

Some short notes of six male cases of inguinal adenitis seen at Soetrang which the author places under the denomination "maladie de Nicolas-Favre." They are, however, no more than clinical cases of climatic bubo without any proof as to their nature. A number of cases presenting lesions in and about the genito-ano-rectal area were also seen. These are very suggestive of poradenolymphitic infections but no tests were made.

H. S. S.

HAUSER (Walter). Die Behandlung der klimatischen Bubonen mit Pyrifer. [**Treatment of C.B. with Pyrifer.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Feb. Vol. 39. No. 2. pp. 68-70.

The author gives the results obtained by treatment with pyrifer in 25 cases.* A course consists usually of 5 to 9 injections at 3 to 5 day intervals. In approximately half the cases good results were seen. In 8 of them retrogression took place without fistula formation, in 4 incision was necessary. The treatment needed 17 to 119 days, i.e., a shorter duration the author thinks than by other methods. In some cases rigors accompanied the rise in temperature; in one case treatment with pyrifer had to be discontinued on account of collapse produced.

H. S. S.

PRYN (R. H. C.). **Climatic Bubo and its Treatment.**—*Jl. Roy. Army Med. Corps.* 1934. Oct. Vol. 63. No. 4. pp. 254-257.

Some notes upon cases of C.B. treated in China and India. In early cases preference is given to protein shock therapy (T.A.B.

* The *Medical Annual*, 1932, states that:—"Pyrifer is a suspension of non-pathogenic organisms sold in strengths varying from 50 to 5,000 millions per cubic centimetre."

vaccine intravenously) and aspiration. In cases in which incision is necessary or sinus formation has occurred he advocates packing with B.I.P.P. The author states that he has had no experience with more recent methods and there is nothing new in this article. H. S. S.

LEVADITI (C.) & LEVADITI (Jean). Certaines formes de tabès sont-elles dues au virus de la maladie de Nicolas et Favre (lympho-granulomatose inguinale)? [**Are Certain Forms of Tabes due to the Virus of L.I.?**—*Bull. Acad. Méd.* 1934. June 12. 98th Year. 3rd Ser. Vol. 111. No. 22. pp. 796-896. With 9 figs. [10 refs.]

The authors recite the results of experimental work devised to test the thesis put forward by JONESCO-MIHAESTI and his colleagues that the virus of L.I. injected intraperitoneally tends to localize itself in the central nervous system with the production of changes resembling those in tabes dorsalis.

In their two monkeys so inoculated while the virus could be shown to be present in the liver, spleen, glands and bone marrow, the central and peripheral nervous system remained intact. It is believed that the changes in the nervous system described by the Rumanian workers were not due to the introduction of the virus of L.I. but to some other cause, this idea being borne out by the fact that such changes had been found in non-inoculated captive monkeys. H. S. S.

MISCELLANEOUS.

TROWELL (H. C.). **The Medical Training of Africans.**—*East African Med. J.* 1935. Feb. Vol. 11. No. 11. pp. 338-353. [41 refs.]

The author notes that there is much diversity in the systems of training in the territories of East Africa, but all are built up on the belief that the bulk of the medical work will ultimately be performed by natives. He is concerned with training in Kenya. He discusses the conditions which govern training; these depend on the "health scheme," the degree to which Africans can be trained, and the money and personnel available.

He gives an account of the work of GORDON, VINT and others on the mental capacity of the African, with respect to his ability to profit by an advanced course of instruction and compares the findings in East Africa with those of American investigators; the conclusions of these are shown to differ.

Under aims and methods of training he describes the various types of training, of dressers, hospital assistants and health workers. Some dressers have proved competent to perform much of the nursing care of patients, but the best require frequent supervision and their knowledge is limited. The hospital assistant is trained in the wards of the native hospital to become in time a competent nursing orderly; the course lasts five years. Health workers have been trained since 1932 at the Jeanes School, Kabete, the original design being that in the morning they should act as dispensary dressers and in the afternoon as district health workers. This for reasons which are stated* did not work and they are now trained purely in preventive medicine and made responsible to the sanitary inspector.

The author then considers the obstacles which bar progress, those of language, philosophy and character.

The lingua franca, Swahili, is foreign to both teachers and taught, and both have but a defective knowledge of it so that it is impossible to convey anything but the most simple ideas. Between the culture and philosophy of the primitive African and that of the twentieth century there is a great gulf.

"The African child is reared in a culture so totally different that it is difficult to conceive of it. He does not move in a world of cause and effect explained in scientific laws, a world whose history is known, whose evolution is gradual, where at the moment the ideals of Humanism supplement the strong edifice of materialism. The African child is reared in a world where ghosts are more real than men, a world in the control of the spirits of the dead. Magical conceptions and magical causation are the only facts of his philosophy. The pleasure or anger of the spirits are the cause of all disease, famine, death, and the whole range of natural science. That being so, to discuss any phenomenon in terms of observation and deduction, is to follow a path of thought which to their minds can only be

* When the author writes—"It is feared that in certain cases he [the health worker] merely made a noise like a sanitary inspector on his way home"—one wonders whether he was shooing the rats or propitiating the spirits of which he lives in dread.

described as insane. The world is full of dreadful forces, the spirits are lurking everywhere, one's attitude to all phenomena is not one of curiosity, observation and deduction, the answer can never lie that way. For the seen is never explained by the seen, always by the unseen. . . .

"If he ever really understands that it is absolutely necessary to weigh and measure the medicine because the effect is proportional to the cause, he must abandon the idea around which his life has previously revolved, that medicine works by reason of some magical power that bears no relationship to its weight or volume."

Finally practically all the failures that have occurred during or after training have been due to want of character. [A lack so well known that this statement requires no elaboration.] A. G. B.

CONGO BELGE. Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes du Congo Belge. Rapport annuel 1933. [**The Activities of Foreami in Belgian Congo in 1933.**—65 pp. With 3 folding maps. Bruxelles: 9a Rue des Petits-Carmes. [Abridged summary appears in *Bulletin of Hygiene.*]

This is the third report of the foundation named Foreami (*Fonds Reine Elisabeth pour l'Assistance Médicale aux Indigènes Congo Belge*). The first and second were reviewed in this *Bulletin*, Vol. 30, p. 569, and Vol. 31, p. 735 [see also p. 326], where some details were given of the genesis of the Institute and of its funds. The present report consists of a preface, a report by Dr. DUPUY, Director of the Sector Bas-Congo-Kwango and another by Dr. PRATI, in charge of the sleeping sickness campaign in Ruanda-Urundi. There are three good maps at the end of the brochure.

The program of Foreami envisages complete medical assistance to natives in rural areas in Belgian Congo. Its chief object is their increase and growth both qualitative and quantitative. It wages therefore a systematic war against morbidity and mortality and comprises the protection of the pregnant woman and young mothers, health education of the people, and preventive measures against endemic and epidemic disease. It visits and examines individually all the natives of a determined region, and seeks out and cares for all persons attacked by diseases which it has set out to combat. It studies also the native's habitat, applies the proper health measures strictly and advises and treats pregnant women and mothers as well as their babies. It is necessary, therefore, to visit every hamlet and village, hut by hut, to register each individual and to preserve medical files for each person and sanitary files for each locality. It provides rural dispensaries, consultations for the mothers and children and hospitals for those who are gravely sick. Such action could not be carried out at once all over this huge colony. It was decided to proceed by stages, to occupy one region for a sufficient time and then to move on to another. The District of Bas-Congo was the first selected, with Dr. DUPUY in charge, and it was divided into 8 subsectors, each under one or more doctors. The personnel of religious missions, professional and lay, as well as of commercial companies of the region was brought into the scheme. The area has now been extended to include part of Kwango, and it is expected that in the course of 1935 the whole of Kwango will be under Foreami and that Bas-Congo will revert to Government care.

						Number of natives	Expenditure
							Francs.
1931	384,799	2,386,617
1932	568,545	6,368,615
1933	634,068	9,772,298
1934 (est.)	770,000	10,894,395

[Ten million Belgian francs would in sterling amount to over £57,000.]

The table shows the progress of Foreami.

The foundation gives also an annual subsidy of 250,000 francs to fight sleeping sickness in the mandated territory of Ruanda-Urundi, 25,000 francs to the Red Cross at Leopoldville for anti-venereal measures there, and 175,000 francs to the Red Cross towards the cost of a research laboratory for leprosy in the Province of Stanleyville. The Administrative Council appeals to Belgians for donations and legacies to help on the work.

The area on which Dr. Dupuy reports extends roughly from the sea to the Kwango river and is larger than Belgium. His report (p. 11-61) is stuffed with figures; it is not suitable for summary but some extracts may be given. He notes that sleeping sickness has regressed by half in two years. He refers to an experiment of two years' duration in which 4,000 babies received a daily dose of quinine with such encouraging results that it is to be extended to all the babies in the sector. He is aware of the objection of the loss of early immunity. A report on this experiment will be of much interest. He refers in two places to the difficulty of bringing medical care to scattered villages or hamlets and the need for regrouping them so as to permit of proper control. The extent of the sleeping sickness problem in the sectors may be gauged from the statement that 12,285 patients were treated in the year.

Under general mortality it is noted that among the 588,148 natives registered there were 13,669 deaths or 23.2 per mille. A table is given comparing the rate at various age periods with that of Europe, presumably Belgium.

			1 day to 3 years	3 to 15 years	15 to 45 years	45 years and over
In Africa p.m.	98.81	9.56	14.38	47.12
In Europe p.m.	49.16	2.216	5.48	36.65

The infant mortality is given as 17.5 per mille.

Dr. PRATI's report is a short one and does not add much to that of the preceding year [see this *Bulletin*, Vol. 31, p. 736]. There were detected in 1933, 850 fresh sleeping sickness cases, an index of infection of 1.3 per cent. or, including old cases, 2.3. As before, the new cases are chiefly in the north, not near the Tanganyika border. The chief administrative measure is a regrouping of the population at a distance from tsetse-infested places.

A. G. B.

CONGO BELGE. Rapport sur l'hygiène publique au Congo Belge pendant l'année 1933 [VAN HOOFF (L.), le médecin en chef a.i.]. [Report on Public Health in Belgian Congo, 1933.]—60 mimeographed pp. With 2 maps & 2 charts.

[Belgian Congo comprises an area of 909,654 sq. miles and has a native population of 9,383,000, *i.e.*, it is $2\frac{1}{2}$ times as large as Nigeria and has less than half the inhabitants.]

Though there was a diminution here as elsewhere of financial resources the medical effectives were fairly maintained in 1933. The figures of the staff are difficult to follow, but it appears that there were at least 10 medical directors, 6 bacteriologists, 6 sanitation officers, and 109 medical officers, and that the subordinate European staff numbered 151. Another table gives 143 doctors and 165 lay personnel. It seems that there is difficulty in recruiting young Belgian doctors, as well as men suitable for the senior and special posts, and that progress is thus held up.

Besides the Government doctors there were five Fomulac doctors [see this *Bulletin*, Vol. 28, p. 763], 3 Red Cross, 8 State missions, 25 foreign missions, 56 private or attached to commercial companies. The black personnel numbered 246. The available money, which amounted to 95 million francs in 1930, was in 1933, 68 millions, but an additional 9 millions was furnished by Foreami [see above] this does not include the mandated territory of Ruanda-Urundi.

The mortality figure for Europeans was 171, the lowest for 9 years, *i.e.*, 9.72 per mille (population 17,588): births numbered 413. The proportion of women to men has been for the last three years 41 per cent. (missionaries excluded). Of the 171 deaths the causes of 108 were known: 12 were from malaria, 13 from blackwater fever. 55 Europeans were invalided, 14 for malaria and its sequelae. The natives treated in the year numbered 580,650, the largest on record, but sleeping sickness, yaws and leprosy are not included here, nor those treated in rural dispensaries. From the figures of Foreami in Bas-Congo the African mortality is put at about 23 per mille. Statistics are given for Leopoldville only:—

Year	Popu- lation	Births	Per 1,000	Deaths	Per 1,000	Excess	
						Births	Deaths
1929 ...	47,000	380	8.6	930	19.5	—	550
1930 ...	39,460	356	9.1	914	23.15	—	558
1931 ...	34,568	378	10.9	679	19.60	—	301
1932 ...	28,806	354	13.0	293	11.08	31	—
1933 ...	27,094	699	25.7	327	12.06	372	---

The number of natives treated in hospital in the colony was 51,117, also a record. Figures are given of natives treated by Government missions.

Epidemic Diseases.

Variola.—There were 3,088 cases, 3,075 of which were "alastrim" or variola minor: of 8 deaths 6 were due to variola major; 283,000 natives were vaccinated with 73 per cent. of success.

Yellow Fever.—No cases reported this year. The result of mouse protection tests went to support the hypothesis of "an old endemic

disease of the Congo basin dating back 20 years, of slow advance and without dramatic expansion" [see this *Bulletin*, Vol. 31, p. 831].

Plague.—No case at the ports and only one in the Albert Lake district.

Typhoid.—Only 10 cases.

Bacillary Dysentery.—414 cases with 104 deaths were reported, an improvement on previous years attributed to prophylactic measures and especially vaccination.

Trachoma appears to be not infrequent in Upper Katanga. 449 cases were treated at Elisabethville.

Of *Undulant Fever* there were 3 suspected cases.

Infectious Jaundice.—In the preceding year there was a small epidemic in Europeans at Stanleyville [see this *Bulletin*, Vol. 31, p. 92], which laboratory examinations have since confirmed as Weil's disease. An epidemic of 614 cases in another part of the Congo was neither Weil's disease nor yellow fever.

Malaria.—1,230 cases and 8 deaths in Europeans. The incidence and fatality have varied little in 5 years. The disease was most prevalent in the Elisabethville Province. Many cases are of course not seen by doctors. *A. gambiae* is the chief vector. There were 55 cases of blackwater in Europeans with 9 deaths, against 72 and 19 in 1932; more than half occurred in the Leopoldville and Elisabethville provinces. The index of malarial infection in natives varied from 6 in schools where quinine was distributed to 80 per cent. No figures are given of microscopical diagnosis.

Trypanosomiasis.—Twelve European cases were detected in the year against 7 in 1932, 9 in the Leopoldville Province. No less than 3,572,423 natives were examined; 27,939 fresh cases were detected and 93,954 old cases were treated. The index of new infection was 0.78 per cent. (0.75 in 1932), varying between 0.16 per cent. in Stanleyville Province and 1.6 in Leopoldville Province. Over 96,000 old and new cases were treated by the Government missions. Since there is no increase of cases the situation is regarded as satisfactory. More and more cases are found to be resistant to the usual remedies, especially trypanamide. It has therefore been decided to give higher doses than 2 gm. and to employ more than one drug. A hatched chart shows the percentage of infections in the various regions. Details of incidence are given for each Province, mission, etc.

Tuberculosis.—21 cases among Europeans; it is suggested that the medical examination undergone before admission to the Congo Belge should be more strict. In natives 817 cases and 360 deaths: the previous highest was 670 in 1931. A number of cases were also reported by the State missions and private doctors. In the Colony generally the disease increases in chronicity and the native race becomes more and more tuberculized.

Of *Pneumonia* there were 4,963 cases with 881 deaths, a fatality of 17.8 per cent.

Syphilis.—8,967 cases were reported in natives, of which 3,713 were primary (accidents primaires), 4,817 secondary and tertiary, 305 congenital and 132 nervous [a surprisingly large proportion of primary syphilis in natives].

Yaws.—42,260 cases were treated in natives and a larger number by missions and other bodies. Yaws is said to be regressing in areas where the medical occupation is "dense."

Leprosy.—Government doctors treated 3,331 cases.

Relapsing Fever.—224 cases in natives, chiefly in Leopoldville and Elisabethville Provinces; 12 cases in Europeans. *O. moubata* is more widespread than was believed. [From the mention of this tick it is inferred that the fever was tick-borne and not louse-borne.]

Endemic Goitre.—1,951 cases were treated, 1,514 in the Stanleyville Province: a number of other foci are mentioned.

Of *Amoebic Dysentery*, there were 63 cases in Europeans and 2,810 in natives; Mayumbe is an important focus.

Of *Ankylostomiasis* there were 24,047 cases.

Schistosomiasis.—15 cases of rectal schistosomiasis were treated in Europeans, 11 of them in the Costermansville Province. In natives there were 3,358 cases of schistosomiasis, chiefly from the Provinces of Stanleyville, Costermansville and Elisabethville. Details are given of the distribution of vesical schistosomiasis, which is more widespread than had been believed. The most important foci are in Elisabethville, where both forms are found.

Filariasis.—Information is given of the distribution of onchocerciasis, which depends on that of simulum.

Ulcerative Rectitis.—Two foci are known in the Provinces of Lusambo and Coquilhatville respectively.

Of *Tropical Ulcer*, 21,457 cases were treated.

A section follows on Medical Assistance to the Natives in which the activities of Foreami, private companies, the Red Cross, Fomulac [see this *Bulletin*, Vol. 28, p. 763], State missions, foreign missions, rural dispensaries, the hospital boat "Belgique" are described. Foreami is described elsewhere in this number (above). Details are given of the work of the rural dispensaries. Under the heading Protection of Native Children we learn that there are 118 infant welfare centres, usually organizations of religious missions, with an average attendance of 16,313.

Some figures are furnished for the schools of native *infirmiers* at Leopoldville, Coquilhatville, Elisabethville and Stanleyville. It appears that 22 passed the examination at the close of the 3rd year.

Under Hygiene of Towns and Stations it is pointed out that the diminution of population both European and native in conjunction with financial stringency has made the maintenance of hygienic services more difficult. At Stanleyville and Coquilhatville the *médecin hygiéniste* has given place to *agents sanitaires*, an effort to put this work on the *médecins des laboratoires* having been frustrated. The essential defence of the Colony, *i.e.*, the services at the ports, Leopoldville, Elisabethville and Albertville has been well maintained. Details are given of the principal places and it is noted that the Europeans of Boma have gone down from 682 in 1929 to 226 in 1933.

Under Industrial Hygiene the great reduction of workers is noted. In Leopoldville Province 10,598 were employed with a mortality of 4.7 per mille (7.2 in 1932): at the Kilo-Moto Mines 26,240 with mortality 4.5 per mille. In Elisabethville Province the effectives have fallen from 16,726 in 1928 (mortality 32 per mille) to 4,281 with mortality 7.01: here it is said that the workers were old boys of the company who were well acclimatized.

The Report closes with a number of tables. From two of them it appears that there are 331 hospital beds in the Colony for whites, and 3,867 for natives.

A. G. B.

WAKIL (A. W.). **A Sanitary Review of the Egyptian Village. Its Present and Future.**—*Jl. Egyptian Med. Assoc.* 1934. Nov. Vol. 17. No. 11. pp. 872-885. With 4 figs.

A paper read at the Luxor Congress by the Asst. Professor of Hygiene, Cairo.

Twelve-and-a-half millions of the estimated population of Egypt (15,200,000) live in the villages, *i.e.*, 82.4 per cent. Of these 75 per cent. suffer from one form or other of schistosomiasis, and 50 per cent. from ankylostomiasis. In one district 40 per cent. of the inhabitants of many villages have oriental sores. Pellagra is common especially among children of 5-15 years; it decreases as one goes south. Sufferers from tuberculosis have been estimated at 200,000 to 300,000, and cattle are infected in the proportion of some 40 per cent.; fortunately boiling of milk is usual. Of 11,717 children examined by the Ophthalmic Section in 32 primary schools only 921, *i.e.*, 7.9 per cent., were found free from trachoma; of patients seen at ophthalmic hospitals 8.4 per cent. are blind in one or both eyes, and in three-fourths of these conjunctival inflammation was the cause.

These are the endemic diseases, and epidemics of typhus, relapsing fever, plague, smallpox, cerebrospinal fever and measles are frequent. The death rate in Alexandria has fallen in thirty years from 33.7 to 26.3, but in the whole country it has hardly moved in this period; in the quinquennia 1901-5 and 1926-30 it was 25.3 and 25.8; improvement has occurred in the towns but not in the villages.

The poverty and ignorance of the fellaheen are measured by the fact that 72 per cent. of peasant males over 5 years of age possess no land, and only 13.7 per cent. can read and write. The insanitary state of the villages is described, and the houses shared by buffalo and donkey.

The author now turns to the future. He considers that the present Egyptian village is beyond redemption and must be replanned. A sufficient area of land must be obtained in its neighbourhood and new building prohibited in the old village; animals would be stabled in their own sheds. He gives a plan of a one-storied house which he calculates would cost £75, the walls to be of burnt brick or masonry, limewashed and the floors cemented. Assuming that 2½ million houses are wanted, a rough estimate gives 200 million pounds as the sum needed for rehousing the Fellaheen. He suggests this might be spread over 50 years. Other problems are the provision of a pure water supply and conservancy. Of the possible sources of water, the Nile and deep wells, he prefers the Nile but the water must be sedimented, filtered and chlorinated. For reception of excreta he discusses the pail system and the concrete vault sanitary privy as used in Tennessee; the bored hole latrine is unsuitable owing to the liability to overflow with the rise of the subsoil water.

Other suggestions for improvement are—the employment of sanitary inspectors instead of barbers to examine into deaths and vaccinate and for other usual purposes; the employment of a health visitor for each village, who would replace the native midwife; the provision of a small clinic where a doctor would attend once a week; the provision of an elementary school for each village; village councils to look to the village sanitation.

A. G. B.

DREYFUSS (A.). Étude géographique et médicale de l'annexe de Laghouat. [**Geographical and Medical Study of the Annexe de Laghouat.**].—*Arch. Inst. Pasteur d'Algérie*. 1934. Dec. Vol. 12. No. 4. pp. 485–547. With 1 map & 12 figs. on 6 plates. [Refs. in footnotes.]

The Annexe of Laghouat lies due south of Algiers between 0·1 and 2·1° E. longitude and 32·9 and 34·5° N. latitude. The Annexe of Ghardaia, or Mزاب country, lies immediately to the south. [For a similar account of this see above, p. 62.] Here are described the country, its inhabitants, products, native and European medical services, and diseases. The author has resided there from 1932 to 1934.

The country is mountainous in the north, reaching 1,400 metres, flat in the south, 700–800 metres: the town which is intermediate lies at 750 metres. The climate is hot in summer and cold in winter, frost being not very infrequent. The population is 21,962, formed of Arabs (about 21,000), Jews (500) and Negroes (200); the Europeans number about 600. The Arabs again are divided into the indigenous Berbers and the conquering Arab race.

European Medicine.—There are two military medical officers who look after the military hospital and the native infirmary, which is the finest in South Algeria: the patients seen here each month number between four and five thousand, women forming about half. *Eye Diseases* furnish more than half the complaints, in the summer especially acute conjunctivitis. Trachoma is common; of 632 children examined 422 were affected. The treatment consists chiefly in washes of sulphate of copper. *Syphilis* comes next. All the forms described as "Arab syphilis" are seen, and other more obscure forms the cause of which is revealed by serology. Interstitial keratitis is common. Primary lesions are seldom seen, but more than half the cases are congenital. The most used drug is acetylarsan. *Gonorrhoea* is frequent with its complications and sequelae, purulent conjunctivitis and arthralgia as well as vaginitis in small children; gonorrhoea is not regarded as a disease. After some remarks on *rickets*, which seemed to be considered here as of syphilitic origin, the author passes to *acute gastro-enteritis*; of 91 babies dying in 1933 in half this was the cause. *Acute respiratory infections* are common, attributed to scarcity of clothing in cold weather; this is the second cause of infant mortality. *Tuberculosis* is very common: one-third of hospital patients have either tuberculous glands, periostitis or osteitis, Pott's disease of the spine, or arthritis, peritonitis or pleurisy. Pulmonary tuberculosis is common: of 114 sputum examinations 30 showed *Myco. tuberculosis*. The tuberculin index based on 1,811 cutis reactions is one of the highest in the Sahara, 58 per cent., 49 for children up to 15, and 70 for adults. The cause seems to lie in the return home of old soldiers and sick labourers. B.C.G. is being administered in the Annexe.

Passing over a number of epidemic diseases we come to *malaria*. This does not now exist at Laghouat itself. Anopheles are not found and the splenic index in schools is nil; it is present however, in an outlying district, parasites having been found at the Pasteur Institute, Algiers, in blood from two persons who had never left the country. *Typhoid* has disappeared with the provision of a supply of potable water. *Typhus* has always been present; an epidemic in 1920 which followed a famine was deadly. Lice are so common that it is usual

for the doctor to find one on his clothing. At present the disease is not in evidence. *Oriental Sore* has several times been demonstrated; *P. papatasi* is found.

Flies are numerous in the summer and swarm on small children's eyes. The mosquitoes found are *Culex pipiens* and *Theobaldia longiareolata* and 7 species of *Phlebotomus* are reported. Scorpions and horned vipers have caused death in the Annexe but not in the author's experience. He has seen syphilitic hemiplegia and paraplegia but never tabes; he has also seen Parkinson's disease in two native shepherds.

Summing up, he points out that malaria, smallpox, typhoid and typhus, formerly prevalent, have disappeared, owing to measures carried out by the health and local authorities. The country is now healthy, but two scourges remain, tuberculosis and syphilis.

A. G. B.

FAST (Johann). Krankheitsbilder aus Java. [Diseases seen in Java.] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 112-116.

The diseases discussed are (1) chronic ulcers, the result of tropical ulcer, yaws or syphilis. Persons with ulcers which would not heal were treated thus—The femoral artery was laid bare as in sympathectomy* for 10 cm. and painted with a 0.4 per cent. phenol solution. This was usually effective [presumably in leg ulcers] and became quite popular. Eventually no chronic ulcers were admitted to hospital unless consent was given to operation, which is described as amazingly effective. Other conditions described are (2) urethral stricture, very common; and (3) liver cirrhosis "after malaria," which begins with splenomegaly in childhood and goes on to ascites and anaemia; recovery is rare. The rest of the paper deals with complications of childbirth.

A. G. B.

VAN DRIEL (B. M.). De sterfte der ondernemingsarbeiders in de Buitengewesten van Nederlandsch-Indië in 1931 en 1932. (Death Rates and Causes of Death among 404,983 Estate Labourers in the "Outer Provinces" of the Netherlands East Indies in 1931 and among 313,790 Labourers in 1932.)—*Meded. Path. Lab. t. Medan-Sumatra.* 1934. No. 14. 175 pp. With 11 figs. [59 refs.] English summary. [Summary appears also in *Bulletin of Hygiene.*]

This report follows the lines of previous issues (reviewed at length in the *Bulletin of Hygiene*, Vol. 6, p. 750; 871; Vol. 7, p. 559; Vol. 8, p. 403). For the East Coast of Sumatra and Atjeh, the corrected rates of mortality on male Javanese show an improvement; the rate in 1932 was the lowest since 1927, viz., 5.80 per 1,000. The rates on Javanese women and on Chinese were lower than in 1931 but above the rates of 1927. Mortality from typhoid fever, malaria and dysentery decreased from 1930; the author attributes this rather to

* According to G. JEFFERSON (CHOYCE's System of Surgery, 3rd Edition, Vol. 3, p. 324) the operation of periarterial sympathectomy has been advocated by R. LERICHE for ulcers and other conditions for some years; it consists in stripping the sympathetic coat of the vessels at the root of the limbs. JEFFERSON says it is not founded on sound principles and will be abandoned. If, however, the operation is effective as appears to be the case (*C. R. Acad. Sci.* 1935. Vol. 200. p. 1156) it is perhaps the underlying theory that must be dropped.

a periodic movement, together with a lower rate of immigration, than to more specific factors. As usual, tuberculosis is the most important cause of mortality; this cause is responsible for about a quarter of the mortality of Javanese males and more than a third of the mortality of Chinese. On the whole, indeed, the mortality rate on Chinese is much higher than on Javanese (the respective rates per 1,000 were 11.94 and 5.8). There is only one important exception to the rule, *viz.*, cirrhosis of the liver, which affects the Javanese much more than the Chinese. The Javanese are total abstainers and suffer very rarely from syphilis. Details are given of the "outer provinces" exclusive of the East Coast of Sumatra and Atjeh because the occupational distribution is widely different; many are employed in mines. The results are similar to those found in South Africa. Thus tuberculosis and diseases of the respiratory system are now found to be more fatal among Javanese than among Chinese. The former are underground, the latter surface workers.

The author remarks that "it would be of much interest, of course, to compare our data with those obtained in other parts of the tropics. The difficulty is, that, as far as the present writer knows, there does not exist in any part of the tropics a statistical report on death rates and causes of death among labourers of the same bulk as ours."

[Discreditable as the fact may be to an even greater colonial power than the Netherlands, we fear it *is* a fact.] *M. Greenwood.*

REED (E. U.). **Medical Observations in the Tropics.**—*U.S. Nav. Med. Bull.* 1934. Oct. Vol. 32. No. 4. pp. 463–467.

The tropics in this instance are certain American-administered islands in the South Sea.

After some remarks on syphilis and yaws, which from his experience in Samoa, Haiti and Guam the author believes to be the same disease, he turns to the relative absence of gonorrhoea in these islands and the presence of conjunctivitis. No sailor contracted gonorrhoea or syphilis in American Samoa during his tour of duty nor did he see cases in the native hospital, but Samoan conjunctivitis, spread by contact and flies, was very prevalent: the causative organism is an intracellular, Gram-negative diplococcus "quite similar to the gonococcus." In 1923 HUNT reported that for two years there had been no severe epidemics of conjunctivitis, but gonorrhoea was "not uncommon." The author concludes:—

"It therefore seems reasonable to believe that these repeated attacks of Samoan conjunctivitis protected the Samoans against gonorrhoea of the genito-urinary tract until the recurring conjunctivitis attacks were greatly reduced in number and severity by treatment with the silver preparations."

[Further study of the organism of Samoan conjunctivitis would help to a decision whether these diseases are related or not. Gonorrhoea is rare also in some British possessions in the Pacific.] *A. G. B.*

HIYEDA (Kentaro). **Distribution of Parasites and Parasitic Diseases in Manchoukuo.**—*Jl. Oriental Med.* 1934. Oct. Vol. 21. No. 4. pp. 39–56. With 3 charts & 1 map. [47 refs.]

The author who is Professor of Pathology, Manchuria Medical College, gives a short account of the parasitic diseases of China in which is found the statement—"The Chinese in the epidemic area do

not consider kala azar a disease but a natural occurrence experienced by everybody."

The most important parasitic diseases in Manchukuo, he writes, are amoebic dysentery, kala azar, malaria and rickettsiasis. Little is known about *amoebic dysentery* here. In 1933 at the Mukden hospital, of 307 dysentery cases 105 were bacillary, 75 amoebic and 21 mixed. From 21 to 38 per cent. of Manchurian labourers are stated to be cyst carriers. The author thinks that nearly half the dysentery in Manchukuo is amoebic.

For *malaria* he gives figures from 15 stations for 6 years, but explains that these cases were in Japanese because the Manchurians do not come to hospital. He would expect the malarial incidence in Manchurians to be higher. In two stations, Fushun and Anshan, there has been a marked increase; in Fushun the result of imperfect drainage of extensive coal mines. The malaria is described as "tertian"; the carriers are *A. sinensis*.

Kala azar.—A map shows how widespread is this disease—"one of the most important endemic diseases in Manchukuo."

Of other intestinal protozoa *Entamoeba nana* is stated to be most common, averaging 41 per cent. Giardiasis is found in 25 per cent. of Manchurian school-children.

Of *helminthic diseases* ascariasis is widespread, ankylostomiasis is common in the southern parts and rare in the north. Since the Manchurians do not go bare-foot it is believed that oral infection is common. The infection is not regarded as grave. Trichuris is also common. *Clonorchis sinensis* was found only twice in Mukden but in 5 per cent. of stray dogs.

Investigation was made of the part played by vegetables in the spread of parasitic infections. Eggs of Ascaris and Trichuris were found. It was concluded that lettuces, which are not easily washed, are most dangerously contaminated.

A. G. B.

CILENTO (R. W.). **Australia's Orientation.**—*Health Bull.* Melbourne. 1933. July-Dec. Nos. 35 & 36. pp. 1039-1066. With 6 figs. [17 refs.]

Australia's orientation in Dr. Cilento's view should be and will be to the north, or, as he puts it, from the sub-tropics to the tropics of that continent.

Dealing with the history of settlement in Australia he indicates the struggle between tradition and experience, tradition holding the settlers to the coast and enterprise and subsequent experience taking them inland to raise sheep and grow wheat; enterprises which, he shows, depend on rainfall as illustrated by the isohyetal lines given on his map. All the early colonization was in the south, and when the Australians expressed opinions adverse to the colonization of the north they overlooked the fact that southern Australia is really sub-tropical and not comparable with England. This is demonstrated by superposing the map of the country, latitude for latitude, on Europe and Africa, Asia and America in turn. Europe is touched at the Spanish peninsula but almost the whole of Australia lies on northern Africa. Similarly in Asia, China, Indo-China and Burma are covered, and in America, Mexico from Florida to Panama. "Latitude for latitude we find Australia superposed not upon Europe but upon northern Africa—upon south-eastern Asia—and upon Central America

and the hotter parts of the United States." One-third of Australia has a rainfall of less than 10 inches but practically all this arid area lies south of the tropic of Capricorn.

BARKLEY basing his estimates on the figures found west of the Mississippi anticipates for Australia a population of about 30 millions, of which 11·3 millions will occupy Queensland and 5 millions Western Australia; *i.e.*, a 13 and 14-fold increase in these States. The population of Queensland has increased in 87 years from 22,300 to nearly a million.

The author thinks that the development of Tropical Australia is inevitable, and again meets the objections raised on the head of "climate."

The actuarial opinion is cited, that there is no need for life assurance offices to treat proponents who live in N. Queensland differently from those who live in other parts of Australia. The Commonwealth statistician pointed out in 1927 that for 15 years the infant mortality for the whole country was 7 per cent. higher than that for Queensland. A table of the "average issue of wives resident in Australia at census of 1921" shows a higher figure for Queensland in each age group than for the whole of Australia. An examination of 2,080 N. Queensland children for height, weight, chest circumference, mentality and nutrition revealed no differences from southern children.

"The authenticated figures of the Commonwealth Statistician demonstrate quite conclusively that white men live and thrive within the tropical portion of Australia at any rate, and have done so for three generations; and that white women can, and do, accompany them without any loss of fertility, mentality, or physique. . . ."

"The evidence from Queensland shows that there is nothing in climate to prevent the development of our tropical regions by white labour, and colonization is actually progressing there at present at a more rapid rate in some areas than in any other part of Australia. Where, in the more barren areas, there are drawbacks owing to remoteness of markets, poverty of soils, unsatisfactory distribution of seasonal rain, and lack of transport facilities, development must be slow and costly, but the introduction of coloured labour would offer no solution, and would multiply difficulties. . . ."

"The dense populations of Eastern Asia are a more valuable asset to Northern Australia as a market for produce than as a source of labour. . . ."

One more quotation—"Australia is really a tropical and sub-tropical land, cleverly coerced into the production of the products of temperate climates, free to a large extent from endemic diseases, and increasingly populated by a white race of high standards and culture, which, during three generations, has demonstrated its fitness for residence in the tropics. It seems to me that we may look forward with confidence to successes in the tropical North equal to those which have so transformed the sub-tropical South." A. G. B.

DIOS (R. L.), DE SOMMERVILLE (E. T. W.), BONACCI (H.), ALDAO (A.) & BARBA (R.). Paludismo y parásitos intestinales en el Territorio de Misiones. [*Malaria and Intestinal Parasitism in Misiones.*]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Nov. Vol. 6. No. 4. pp. 458–505. With 2 graphs, 2 maps & 9 coloured plates.

The territory of Misiones (Argentina) lies south-east of Paraguay. The authors examined a number of blood films for malaria parasites and faeces for helminthic or protozoal infestation. [Evaluation of the

results of the former is somewhat difficult for the figures vary; in one place it is stated that 4,959 specimens were examined, in another 5,489, and on this last the authors' percentages are based; in a detailed protocol of 20 localities the total examined is 4,985. As this is the most detailed we will adhere to it.] Of the 4,985 specimens 879 or 17.6 per cent. were positive; 710 contained *P. vivax*, i.e., 80.7 per cent. of those positive, and 123 or 13.9 per cent. *P. falciparum*; there were 50, or 5.6 per cent., of mixed infections; quartan was not found at all [it will be noted that these total 883]. In the authors' protocol summing up the results there were 1,024 positive out of 5,489 or 18.6 per cent. and of these 786 (76.7 per cent. of the positive) were benign tertian, 174 (17 per cent.) subtertian and 64 (6.2) mixed.

As regards the second part of this article, the number of faecal specimens examined is not stated, but 166 were found positive. In a more detailed table 11 districts are mentioned and the percentage findings of helminthic ova, alone and combined, are given. Protozoal findings comprised only *E. coli* and *Giardia lamblia*. The percentage figures alone, based on so small a number, conveys little information of value.

H. H. S.

CLARK (Herbert C.). **The Gorgas Memorial Laboratory and Problems engaging its Attention.**—*Trans. College of Physicians of Philadelphia*. 1934. Vol. 2. No. 2. 4th Ser. pp. 140-149. [19 refs.]

The Gorgas Memorial Laboratory is the tropical subdivision of the Gorgas Memorial Institute, which is situated on the sea coast of Panama City. It has now been five years at work and this paper gives an account of its activities.

Malaria control and equine trypanosomiasis have engaged most of the attention of its staff. The author, who is Director, estimates that the Caribbean negro loses 40 per cent. of his efficiency if left in unsanitated conditions and without medical care. He mentions, however, the difficulties with which tropical fruit companies meet in combating malaria.

"It was believed that with the close of the construction period in the history of the Panama Canal the cost of maintenance in mosquito control would gradually fall due to the permanent obliteration of water surfaces and to drainage. It now proves that as a result of the presence of the artificial bodies of water known as Gatun Lake and Miraflores Lake the need for mosquito control will increase rather than diminish so that the control of malaria must be approached as something to be indefinitely continued."

Five native villages on the Chagres river in the midst of large anopheline breeding beds are now under study, with two others as controls. The antimalarial measures are—mosquito-proofed quarters, short radius mosquito control, and compulsory monthly blood-film surveys followed by treatment of those parasitized with atabrin and plasmoquine. In 4 years the parasite rates have been reduced to about a quarter of the original, but it is difficult to make a further reduction.

Trypanosomiasis.—Twelve human cases of Chagas' disease have been studied, none of them harmful and all found accidentally. The *T. hippicum* infection of horses and mules described by DARLING (1910) is of importance. It is treated with success in some half of the cases by naganol and tartar emetic. It is transmitted by the vampire bat, *Desmodus rotundus murinus* [see this *Bulletin*, Vol. 30, p. 120], which will absorb 16 cc. of blood at a meal. The animal

carriers are cattle ; $4\frac{1}{2}$ per cent. of those ranging with equines are infected.

Relapsing fever.—As recorded elsewhere a spirochaete found in a wild monkey was transmitted to man through ticks as well as direct [see this *Bulletin*, Vol. 29, p. 208].

Reverting to the malaria sanitation of the Canal the author refers to two new features which have recently appeared—a number of native settlers and the two Lakes above mentioned, one of which has 165 square miles of surface and a shore line of about 1,000 miles. In the last weeks of the dry season one side becomes “a massive breeding bed,” and the author suspects that interrupted night flights will carry the mosquitoes to the terminal points of the Zone, *i.e.*, a total flight of 15 miles. The settlers are abundant along the line of flight and their parasitic index is about 25 per cent. Trapping experiments are being made along the supposed line of flight. Another disturbing event is the arrival of three fresh anophelines, *A. albitarsis*, *A. bachmanni* and *A. strodei*.

This is a sample of the work done at the Gorgas Memorial Laboratory from which 47 publications have already been put forth. A. G. B.

MACKIE (Thomas T.). **Tropical Medicine in New York City**.—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 59–65.

Though New York is the headquarters of the International Health Board (Rockefeller Foundation) and of its Yellow Fever Research Laboratories, and Columbia University is affiliated with the Porto Rico School of Medicine, and though tropical diseases are often seen in the large foreign-born population as well as in returned missionaries and emissaries of commerce, affording a large and relatively unexplored opportunity for the study of these diseases, there is no hospital or clinical group giving service to patients thus suffering and hence no facilities for teaching. The author seeks to arouse the interest of the medical profession in America, which at present may be compared with that of the medical practitioners of London when MANSON began his work at the Seamen's Hospital towards the close of the last century.

A. G. B.

RUSSELL (Frederick F.). **The Educational Background for the Practice of Tropical Medicine**.—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 1–9.

The author gives a brief account of MANSON's career with special reference to his teaching in China and in London, the foundation of the London School of Tropical Medicine and its later consolidation with the London School of Hygiene ; he describes appreciatively what has been done in the elimination of beriberi and the control of malaria in British Malaya ; he indicates the lack of training in hygiene and public health in the medical graduate of to-day, and thus leads to this conclusion :—

“The combination of curative and preventive practice which confronts the medical man in the tropics indicates clearly that the student should have all training possible in hygiene and public health, subjects not adequately presented to undergraduate students.

“To make the tropics healthy for Europeans and natives alike, tropical medicine, as a graduate subject, should be taught in close association with schools or departments of hygiene and public health.” A. G. B.

VAN TRICHT (B.). **European Children in the Tropics.** [Correspondence.]
—*Brit. Med. J.* 1935. Mar. 23. p. 620.

Dr. James GARDNER wrote in the *British Medical Journal* of December 1, 1934 :—

" Why is it that English people cannot live in the coast towns of Java the whole year round, but have to go up to the hills part of the year, and have to send their children home to England for their health, whilst Dutch couples will go out to Java, live in the coast towns all the year round, and rear and educate their children there, and maintain their health without sending them home to Holland ? "

Dr. van Tricht writes from an experience of 20 years practice in Batavia. The principle of the Dutch colonizers, he says, has always been to keep up family life. As a rule they keep their children with them till they are 14 or 15. That the British do not do the same is the result of prejudice. The Englishman does not like his children to be born in the tropics and wants his sons to be educated at a public school. In Dr. van Tricht's judgment, there is no medical aspect to the question.

A. G. B.

BLACKLOCK (D. B.). **House Diseases in the Tropics.**—*Lancet.* 1935. Mar. 2. pp. 526-529. [33 refs.]

This was a Chadwick Lecture, delivered in October, 1934. The " house diseases " are, malaria and blackwater, yellow fever, relapsing fever, plague, typhus and kala azar.

In *malaria* the house may be structurally defective so that it cannot be properly screened, or it may be sited within flight range of the anopheline vector, or—a special case—anophelines may breed in water exposed within it. [GIGLIOLI's papers on quartan malaria and blackwater as house infections have been overlooked ; see this *Bulletin*, Vol. 30, p. 97.]

In *yellow fever* neither structure nor site is in question but the presence in or near the house of vessels containing water due, it may be, to the absence of a proper piped supply.

In tick-transmitted *relapsing fever* it is the structure that matters but an improved type of house may harbour the tick vector more than the unimproved ; *e.g.*, the African native's house is a temporary affair and can be abandoned in case of sickness whereas the Arab makes a more substantial residence which gives good harbourage to the vector. In the louse-borne kind overcrowding and personal hygiene are in question.

In *plague* the methods of construction and the materials are of importance, with reference of course to rats. Here again a better house may be worse than a poorer one which gives less harbourage. In India plague prevention is not a matter of expenditure but of domestic hygiene.

In *typhus* as in louse-borne relapsing fever personal hygiene and habits are the important factors. In the endemic form it is the rat that matters.

In *kala azar* the house connexion is not so clear because the precise method of spread is still in doubt. The experience of DODDS PRICE and ROGERS that coolies removed to new lines 400 yards from the old remained free from the disease whereas of 50 who remained in the old lines 16 per cent, died of kala azar is striking, and there is

similar later evidence to the same effect. Whether it is the site or the structure or the habits of the inmates is uncertain.

[There is nothing new here but the presentation is fresh and the importance of housing conditions in the tropics will bear fresh stress.]

A. G. B.

MÜHLENS (P.). *Forschungsarbeiten des Hamburger Tropeninstituts und ihre Bedeutung für die Medizin und Hygiene der warmen Länder. [Researches of the Hamburg Tropical Institute and their Importance for the Medicine and Hygiene of Hot Countries.]*—Reprinted from *Med. Welt*. 1934. No. 39. 12 pp.

The Hamburg Tropical Institute was founded in 1901 and has trained 2,196 doctors. There are 60 beds in the Tropical Hospital. The author gives an account of the principal researches conducted at Hamburg and in the tropics by members of the Institute. The deprivation of colonies in 1919 has not brought the work to an end, for it has continued in South and Central America and elsewhere.

A. G. B.

KNOWLES (R.) & BASU (B. C.). *Mosquito Prevalence and Mosquito-borne Diseases in Calcutta City.*—*Records of the Malaria Survey of India*. 1934. Sept. Vol. 4. No. 3. pp. 291-319. With 11 charts & 1 fig. [38 refs.]

This paper deals with the breeding places of *A. stephensi* in Calcutta and their relation to meteorological conditions, and similarly with the breeding of *A. aegypti* and *C. fatigans*; with *A. stephensi* in relation to malaria, which is so puzzlingly infrequent in Calcutta; with *A. aegypti* in relation to dengue, and *C. fatigans* in relation to filariasis.

The essentials, apart from the graphs, are contained in the summary.

" 1. During a period of four years the density of breeding of *Anopheles stephensi* in the centre of Calcutta city has been kept under close observation in an area one square mile in extent around the Calcutta School of Tropical Medicine. This species of mosquito pullulates in almost every receptacle for water storage throughout the city, especially in masonry tanks and overhead galvanized iron cisterns on the roofs for the filtered and unfiltered water supplies. Out of 11,927 examinations during four years no less than 33 per cent. gave positive results.

" 2. The correlation of the monthly incidence of *A. stephensi* breeding with the meteorological conditions in the city is shown (the latter figures being from the means of twenty years' records at Alipore). The maximum breeding occurs in July and the minimum in April.

" 3. During the same four years the density of breeding of *Aedes aegypti* in the same area has been under observation. The chief breeding sites are the same as those for *A. stephensi*. Out of 11,927 examinations of such sites no less than 41 per cent. gave positive results. The greatest intensity of breeding was found during July and August, and the lowest in February and April.

" 4. The breeding of *Culex fatigans* throughout the same area was observed for two years. The chief breeding sites are the same as those of *A. stephensi* and *A. aegypti*. Out of 4,339 examinations of suspected breeding sites 8 per cent. gave positive results. The greatest intensity of breeding was found in November and the lowest in July.

" 5. Many residents of Calcutta city acquire malaria during visits to the mofussil. There is continuous and heavy importation of malaria into the city by immigration from heavily endemic areas in Bengal. The local

strain of *A. stephensi* can be very readily infected experimentally with malaria. Meteorological conditions for malaria transmission are suitable over a large part of the year. Yet at present malaria is but little endemic in the city. What are the reasons for this discrepancy?

"6. The chief reason for the low endemicity in Calcutta appears to be that the maximum density of *A. stephensi* breeding (July–August) fails to coincide with the chief incidence of malaria cases (October–November), and especially of gametocyte carriers (December). Details are given with regard to all three species of malaria parasite, and conditions in Bombay and Calcutta are contrasted.

"7. The maximum peak of *Aedes aegypti* breeding is in July and August; and this corresponds to the maximum intensity of fresh infections with dengue (August and September). Here the correlation is almost perfect. This accounts for the devastating epidemics of dengue which so often sweep the city and cause enormous financial loss.

"8. New admissions for filariasis are at a fairly uniform rate throughout the year (general filaria rate 9.5 per cent.). The most favourable period for transmission is during the monsoon (July–September), when the intensity of breeding of *Culex fatigans* is at a very low level. The peak for *Culex* breeding is in November, when conditions for filariasis transmission are rapidly becoming unfavourable. This want of coincidence keeps the filariasis rate at a relatively low level.

"9. The cure for this state of affairs is the provision of a continuous water supply of sufficiently high pressure to prevent mosquito breeding in the reservoirs, cisterns, etc., throughout the city. It is the low pressure and intermittent character of this water supply which is responsible for the prevalence of mosquito-borne diseases in Calcutta."

The following passage is found under Remedial Measures :—

"Malaria is not apparently a very serious danger to Calcutta city, but we have already one virulent mosquito carrier—*Anopheles stephensi*—breeding in almost every other water storage receptacle in the city, together with the recent introduction of a second, and even more virulent carrier, *Anopheles sundanicus* (*A. ludlowi*). The future is quite uncertain and it would not be safe to anticipate. Further enquiry is urgently called for (and is at present in progress).

"Dengue is a perpetual nuisance in Calcutta and from time to time it assumes a severe epidemic form. The mosquito which transmits the disease is known, its breeding places in the city have been described, and its eradication ought to be possible. Dengue must cause a very big financial loss to the commercial industries of Calcutta annually.

"Filariasis in Calcutta city is a disease which especially affects the Anglo-Indian and Hindu communities. It is a cause of very much suffering and economic loss among the poorer Anglo-Indian and among Hindu communities. The mosquito which transmits it can be eradicated if measures be taken against the other two species responsible for mosquito-borne diseases in Calcutta.

"The cure for this state of affairs is neither mosquito-brigades nor larvicides, neither kerosene oil nor Paris green. It is the provision of an adequate high pressure and continuous filtered and unfiltered water supply to the city. This is no new recommendation; it was urged by James (1913), Christophers (1915), Iyengar (1920), Basu (1930), and Covell (1932). It is abundantly clear that the main breeding places of mosquitoes in Calcutta city are the reservoirs of filtered and unfiltered water. These constitute such danger as may occur of epidemic malaria from *Anopheles stephensi* breeding; of the frequent and harassing epidemics of dengue which sweep the city; of the very great amount of suffering among the poorer class Anglo-Indians and among Hindus from filariasis. Finally, if by any chance yellow fever was introduced into the city, conditions would probably be more terrible than anything ever recorded in Panama or Central and South America."

A. G. B.

PARKER (R. R.). Recent Studies of Tick-borne Diseases made at the United States Public Health Service Laboratory at Hamilton, Montana.—Fifth Pacific Science Congress. pp. 3367–3374.

Laboratory activities at Hamilton, Montana, have been concerned mainly with the four recognized disease conditions associated with the bite of the Rocky Mountain wood tick, *Dermacentor andersoni*: Rocky Mountain spotted fever, tularaemia, Colorado tick fever and tick paralysis. This paper is concerned chiefly with the first and second, both of which have come lately into prominence, R.M. fever as having been recognized in several central and eastern States as well as in south-west Canada, tularaemia as having been identified in northern countries of Europe and Asia and in Japan.

Rocky Mountain fever is now known in 14 eastern and Mississippi States as well as in 13 Rocky Mountain and Pacific coast States. It is probable that these recently detected foci are not fresh introductions of the virus but that it has long been present in the arachnid and mammalian fauna. It may be that the virus is present in a low-grade phase incapable of provoking other than mild or inapparent infections, and that the virulence in individual ticks may on occasion be raised to such a level as to provoke recognizable infections. These questions are now under study by means of the rabbit tick, chosen because it consistently carries low-grade virus, and is the only tick which occurs wherever spotted fever is endemic, with a range extending still further. Present evidence goes to show that ticks are the only carriers, and the studies made since 1928 incriminate *Dermacentor variabilis*, *D. occidentalis*, *D. parumapertus marginatus*, *Rhipicephalus sanguineus*, *Amblyomma americanum* and *A. cajennense* as possible natural carriers and *D. occidentalis*, *R. sanguineus* and the two species of *Amblyomma* as possible agents of transmission to man. It is considered probable that the virus is equally well adapted to tick species occurring in other continents.

Colorado tick fever.—In many parts of the Rocky Mountain region, most often in Colorado and Wyoming, the febrile reactions so designated follow the bite of *D. andersoni*.

"This disease is of a remittent type and is commonly characterized by the occurrence of two febrile periods, each of two to four days' duration, with a remission period of one to several days between. The onset is sudden and the fastigium is often reached within the first 24 hours. *There is no rash*. Symptoms other than fever are malaise, chilly sensations, severe headache, non-productive conjunctivitis, photophobia, and generalized muscular and joint pains with particularly severe aching in the lumbar region. The malaise is usually intense. Constipation is the rule. The temperature often reaches 104° to 105°F. or over, but may not exceed 101° to 102°F. The pulse rate is frequently 120 to 130. In most instances, though not always, the symptoms are more severe during the first febrile period. It is claimed that occasional cases are seen with one or three febrile periods instead of two. The recurrence of symptoms has sometimes been attributed to a too early attempt to become active on the part of the patient. It is non-fatal."

"The onset is more sudden than in mild cases of spotted fever, the pulse rate accelerates more rapidly, and the fastigium is reached more quickly. The initial malaise and general muscular pains and backache are usually more intense. Also, there is no rash. As noted above, all attempts to reproduce the infection in laboratory animals by blood inoculation (usually easily accomplished from typical cases of spotted fever) have consistently failed, while the sera from blood samples taken during both illness and

convalescence have not agglutinated *proteus* X organisms in significant titre."

For the section on Tularaemia, which contains a summary of the numerous findings in that disease, the paper must be consulted.

A. G. B.

YORKE (Warrington) & MURGATROYD (Frederick). Biological Problems in Chemotherapy.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 435-457. With 4 graphs. [32 refs.]

The discovery of a technique by means of which trypanosomes may be kept alive *in vitro* for at least 24 hours has enabled certain chemotherapeutic problems to be reinvestigated. Trivalent arsenic and antimony compounds have in comparison with pentavalent compounds a surprisingly high trypanocidal activity both *in vitro* and *in vivo*. This suggests that the therapeutic action of the trivalent arsenicals and arsphenamine compounds is dependent on the trypanocidal action of the unchanged drugs, while that of the pentavalent compounds is associated with some previous change, probably reduction, in the body of the host. Nevertheless pentavalent are preferred to trivalent compounds in the treatment of trypanosome infections. This is probably due to a number of factors. When trivalent arsenicals are injected into rabbits the serum is at once endowed with an enormous trypanocidal titre. This high titre does not, however, last long. When pentavalent compounds are injected the trypanocidal titre develops much more slowly. Trivalent arsenicals are also excreted more rapidly in the urine, while pentavalent compounds such as tryparsamide, though rapidly giving rise to a high trypanocidal titre in the urine, are much more slowly excreted. After an injection of tryparsamide into a rabbit, for instance, the trypanocidal titre of the urine only reaches zero after a day or more. A further difference between tri- and pentavalent arsenical compounds is that reduced tryparsamide and neoarsphenamine diffuse rapidly into and out of red blood corpuscles and are unchanged in the process. Tryparsamide also diffuses into red blood corpuscles but is to some extent reduced by the haemoglobin into its highly trypanocidal trivalent form. Other tissues also probably play a part in this reduction.

The essential characteristic of drug resistance is found to be a change in the parasites whereby they do not fix the drug applied *in vitro* as do normal parasites. The development of a resistant strain is fundamentally a mutation, *i.e.*, a gradual change in all or certain individuals resulting from the stimulus of frequent exposures to suitable concentrations of a drug. When once a strain of trypanosomes has become arsenic resistant it retains the character indefinitely. It is not lost when passed for prolonged periods through laboratory animals by means of the syringe nor by numerous cyclical transmissions through the natural intermediate host. The importance of this concept is seen in the fact that arsenic resistant strains of trypanosomes are being obtained in considerable numbers from African natives, probably as a result of the wholesale atoxylization of patients which is now being carried out by itinerant medical missions. Although it is easy to produce strains of trypanosomes resistant to aromatic

arsenicals and antimonials it is fortunately difficult to produce strains resistant to Bayer 205. Experiments are described to show the importance of the size, spacing and number of doses of a drug in producing resistant strains.

G. M. Findlay.

BUCHANAN (J. C. R.) & SANDERSON (Iain). **Ulcers in the Native African. A Further Investigation.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 505–510. With 1 diagram.

This is a continuation of a paper by CONNELL and Buchanan noticed in Vol. 31, p. 337 of this *Bulletin*, in which it was stated that “zipp” (bipp with zinc ointment substituted for bismuth) and a plaster case formed a satisfactory treatment.

Data relative to the patient or the ulcer are given in a table. This shows *inter alia* that while 56 members of the hospital native staff had a Hb percentage of 93·5, in 89·5 per cent. of the ulcer cases the Hb was under 80.

A diagram shows a leg in four aspects on which is dotted the sites of 641 ulcers. These dots merge over the tibia in front, the tendon of Achilles and the malleoli, showing graphically that the main ulcer-bearing areas are situate in areas poorly supplied with blood and exposed to injury.

Three groups of patients were treated (1) ambulatory, 67 cases, as in the first paper, with zipp under plaster, weekly injections of arsenic or bismuth, and mercury and pot. iod. by mouth; (2) 55 cases local treatment as (1) but in bed in hospital with a special diet including cod-liver oil, yeast and iron; (3) 36 cases, as (2), but with “zincera” substituted for zipp once the ulcer is clear (zincera is beeswax 80 parts to zinc oxide 20 parts, heated till soft, spread on lint and closely applied). The results are shown in a table. The dietetic treatment improved the general condition without accelerating healing. In the third group there was such acceleration, and it is this treatment both in and out of hospital which they recommend for up-country use. The time occupied in healing was 25·2 to 36 days according to the area of the ulcer.

A. G. B.

CLUNIE (T.) & EVA (Alokihakau). **Tropical Ulcer in Fiji.**—*Fiji Ann. Med. & Health Rep. for Year 1933.* pp. 34–37.

In 1933 the incidence in Fiji of this condition “assumed almost epidemic proportions.” Clinically it resembles the ulcerative dermatomycosis of Castellani. There was usually a history of a scratch by sensitive grass. There was no tendency to burrowing. The patients came from institutions and road gangs, which suggests to the authors a dietetic factor, for in these bodies white bread and sugar are used to the exclusion of native foods. Treatment was by Dickson-Wright’s method, *i.e.*, strapping with elastoplast at a cost of 1s. 9d. per week, the patient following his vocation, and the average course being two to three weeks. No figures are given of the numbers treated.

A. G. B.

BRENNAN (C. H.). **An Ointment for Use in the Treatment of Ulcers.**—*East African Med. Jl.* 1934. Oct. Vol. 11. No. 7. p. 233.

The author thus describes his ointment :—

" The ointment is composed of :—

Cod liver oil	3 drams
Eusol	2 ounces
Vaseline	1 ounce
Ung. zinci	1 "

" The cod liver oil is put in a bottle with the eusol and well shaken together.

" The mixture is then worked into the vaseline and ung. zinci on a porcelain plate.

" It has been found useful in the 'clean' stage of the ulcer and can be left on for three days, which is an economy in labour and dressings."

A. G. B.

CARMAN (John A.). **A Note on the Use of Tinfoil in the Treatment of Abrasions and Ulcers.**—*Jl. Trop. Med. & Hyg.* 1934. Dec. 1. Vol. 37. No. 23. pp. 376-377.

The author uses tinfoil in superficial abrasions, superficial burns after the initial pain and shock have been alleviated, and ulcers with clean granulating surfaces where skin-grafting is not justified or is refused. The surface is cleaned with saline or boracic, a sheet of "silver paper" is bandaged in position and left undisturbed for 3-7 days. The author does not claim originality for the treatment.

A. G. B.

GIORDANO (Mario). **Un caso di ainhum in Tripolitania.** [**A Case of Ainhum in Tripolitania.**]—*Ann. di Med. Nav. e Colon.* 1934. Sept.-Oct. 40th Year. Vol. 2. No. 3-4. pp. 529-533. With 2 plates. English summary (2 lines).

The case was typical and its chief interest lies in the fact that only four cases have previously been reported in Tripolitania. The patient was a negro, 27 years of age, who first noticed the condition 3 years ago. The author believes that the disease is not very rare, but patients do not all come for treatment and on the other hand some that do are wrongly diagnosed. This, in fact, was diagnosed as "atrophic ulcer of the left little toe" and the W.R. proving positive (though the Kahn and Sach's Citochol tests were negative) the addition "of syphilitic origin" was made.

H. H. S.

IRGANG (S.) & ALEXANDER (E. R.). **Iodide Therapy for Relief of Pain in Ainhum. Report of a Case.**—*Arch. Dermat. & Syph.* 1934. Oct. Vol. 30. No. 4. pp. 508-509.

" A case of ainhum [in a negro from Trinidad] in which severe pain of about ten weeks' duration was the chief complaint is presented. . . . A few hours after a single intravenous injection of 31 grains of sodium iodide, this symptom disappeared; it had not returned fourteen days later, when the patient was last seen."

A. G. B.

KOUWENAAR (W.), MAASLAND (J. H.) & WOLFF (J. W.). Onderzoekingen over het rhinosclerom op Sumatra. III, IV en V. [*Rhinoscleroma in Sumatra.*—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Sept. 25, Oct. 9 & 23. Vol. 74. Nos. 20, 21 & 22. pp. 1285–1304; 1330–1342; 1447–1454. With 60 figs. on 10 plates.

III. Kliniek van het rhinosclerom. [*Clinical Conditions.*] [KOUWENAAR.]

By a study of 53 definite cases the clinical symptomatology of this deforming disease has been assembled. Numerous photographs are included.

The symptoms are summarized as follows :—1. The first subjective symptoms are itching, sometimes pain and later bleeding at the nose. 2. Infiltrations next become visible in the skin of the nose, the upper lip and the interior of the nose. These can extend to the neighbouring localities, are hard as bone, bluish red, usually fairly symmetrical, bleed easily when affecting mucous membranes and are often very painful. 3. Extensions take place to pharynx, soft palate, and tonsils. The uvula frequently is destroyed with marked cicatricial contraction. The lachrymal sac may become involved and a fistula may form in this situation. If the eustachian tube is affected there is tinnitus and deafness. 4. In the Batak lands of Sumatra, as compared with that of Eastern Europe, rhinoscleroma exhibits a much greater localization to nose, upper lip and palate. 5. The lymph nodes below the jaw are enlarged. 6. This affection is a slowly progressive one, which does little harm to the general health. 7. In some cases it is more rapid with production of deforming tumours of the nose and upper lip. 8. Arrest of the process at any time was not observed. Contraction of the tissue with the formation of fibrous tissue may decrease the size of the tumours. Ulceration may later take place and the condition come to resemble gangosa. 9. Women are more frequently affected than men. 10. Clinical symptoms do not appear before puberty and develop usually between the 20th and 35th year. 11. It is possible that true bacillary carriers occur.

IV. Bacteriologie. [*Bacteriology.*] [WOLFF.]

The bacterium which is incriminated as the causal agent of rhinoscleroma was first described by FRISCH. It belongs to the group of capsule bacteria, is named *Klebsiella rhinoscleromatis* and is closely allied to the ozaena bacterium, *Klebsiella ozaenae*. The specific bacillus has been isolated frequently from the rhinoscleroma nasal lesions affecting the Bataks of Sumatra and is here subjected to bacteriological analysis, of which the detail is as follows :—

Gram-negative bacilli, with rounded ends, mostly capsulated, non-motile, producing no gas in any medium; indole-negative; not liquefying gelatin, nail-head appearance in stab culture: endo-plate colony slimy, white or extremely pale rose; agar colony slimy, sometimes irregularly contoured; Rothberger-Oldekop unchanged: no coagulation of milk even after boiling; turbidity in broth, sometimes a slimy ring at the edge: acid formation (sometimes slow) in glucose; lactose unchanged: acid in mannite and maltose: slow acidification of saccharose: reduction of litmus absent; inhibition of growth by bile: litmus whey violet to violet-blue: methyl red reaction positive (red): Voges-Proskauer reaction negative.

The *Klebsiella rhinoscleromatis* does not, while the *Klebsiella ozaenae* and *K. pneumoniae* do, invert amygdalin. These organisms are

serologically differentiated. The specific organism was obtained also from contacts with and the family of patients suffering from rhinoscleroma. The *Klebsiella ozaenae* was also met with in the nose flora of Bataks. An investigation of the nasal flora of Bataks outside the region in which patients were found furnished no cases with the specific organism. A point of interest in the investigation was the great frequency of a faecal nose flora among the Toba- and Karoland Bataks.

V. De waarde der complementbindingsreactie bij het rhinosclerom-onderzoek. [**Value of Complement Fixation Reaction in Rhinoscleroma.**] [WOLFF.]

A complement fixation reaction would, if it were sufficiently specific, be a valuable means of making rapid survey of a population for rhinoscleroma along with clinical and bacteriological examination and of detection of early cases. The present research goes to confirm its specificity although group reactions may be obtained in rhinoscleroma patients with ozaena antigen. Considerable importance is attached to the method of preparing the antigen if clear cut positive results are to be obtained. The method employed was to filter a fresh suspension in normal salt solution of a 24-hour culture through cotton wool, heat the filtrate 1 hour at 80°C., keep it in the ice chest over night, pipette off the supernatant suspension and bring the suspension to a standard opacity for use as test antigen. It is possible that still more specific results may be obtained by using an ether extract and, still more important, a preparation obtained which can be used for about a month. The salt suspension requires to be freshly prepared. In the actual test an excess of complement is used.

The reaction was found to be positive in 92.5 per cent. of the manifest rhinoscleroma cases and in nearly 100 per cent. of the bacteriologically positive cases. Non-specific reactions occasionally appear which represented, in the authors' series of control persons, a proportion of about 1.1 per cent. A much higher percentage (6.7) of positive reactions was, however, obtained by confining the control observations to families and to inmates of the same house or village. Some of these were probably carriers or early cases with no clinical symptoms.

W. F. Harvey.

SMITH (E. C.) & ELMES (B. G. T.). **Malignant Disease in Natives of Nigeria : an Analysis of Five Hundred Tumours.**—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 461–512. With 71 figs. on 18 plates. [24 refs.] [Summary appears also in *Bulletin of Hygiene.*]

So many vague and unsubstantiated statements concerning the incidence of malignant disease in the less civilized races of man have been current, that the collection of data provided in this paper is especially welcome. The examples of cancer in natives here described have been collected from all over Nigeria wherever a medical officer has penetrated.

As the authors point out, there are some essential obstacles to the study of cancer occurring among primitive races. Men attend the hospitals more readily than women and the comparative incidence of the disease in the two sexes cannot be ascertained. Again, with the exception of some non-adults, it is impossible to know the age of a native patient. Nevertheless, and in spite of such inherent drawbacks,

the authors have collected data of great interest and value. They establish indisputably the fact that natives of Nigeria are afflicted with cancer, and thus supply yet one more refutation of the oft repeated though rather foolish statement that it is a disease of civilization. Not the least noteworthy part of their paper concerns the nature and sites of the malignant growths. If the melanotic tumours are counted as sarcomas, the carcinomas and sarcomas occurred in approximately equal numbers—carcinoma, 225; sarcoma, 220; other tumours 55, including mixed parotid tumour (18), endothelioma (17), adamantinoma (13), cylindroma (2), perithelioma (2), teratoma (2), chorionepithelioma (1).

That the incidence of cancer in the various regions of the body differs in the various races of man is well recognized; and the phenomenon is strikingly illustrated in these cases from Nigeria. Of skin tumours there were 94, and of these 39 originated in the foot, 30 being melanomata. There were 55 cases of tumour of the liver of which "32 were undoubtedly of primary hepatic origin," cirrhosis being present in 17 of these primary cases. Among 49 tumours of bone, no fewer than 28 involved the jaws, and of these 13 were adamantinomas. The orbit was a not uncommon site of cancer, being responsible for 30 of the 500 cases analysed. Of these 30 orbital tumours, 10 were round-celled sarcomas occurring in children under 10 years of age. Another rather frequent source of malignant growth was the salivary system, 29 tumours being recorded as affecting the parotid region. There were 25 cases of mammary carcinoma, one of which was in a girl of 15, and three were in young adult males. Curiously enough, in a country where infection with *Schistosoma haematobium* is common, only one tumour of the bladder was seen—a carcinoma—and in this instance there was no evidence of a schistosome infection. The authors saw no instance of cancer of the pharynx, and only one case—in an old man—of cancer of the oesophagus.

They mention a squamous carcinoma of the finger in which "the history is suggestive of a possible occupational factor in connection with the aetiology of the condition," the patient having been an indigo-worker for many years. Judging from the numerous facts collected by the authors in this paper, the native races of Africa appear to offer a fine field for original cancer research. *H. Burrows.*

CHATTERJEE (Tarapada). **Epidemic Dropsy.**—*Calcutta Med. Jl.* 1934. July. Vol. 29. No. 1. pp. 7–16.

This paper contains a full summary of our knowledge of epidemic dropsy as it occurs in Bengal.

The following etiological factors are of importance: Epidemic dropsy is almost exclusively confined to Bengalis in Bengal. No Marwari nor European has ever been affected with the disease. Epidemics occur about the middle or end of the rainy season and as winter comes on the disease disappears. Males and females are equally affected, but the author has never seen the condition in a child of less than 8 years. One attack of epidemic dropsy does not confer immunity, nor does it render persons more liable to a second attack. Though the disease occurs in households, etc., it should not be regarded as infectious.

The actual cause of epidemic dropsy is to be sought in the peculiarities which distinguish the Bengalis from other races living in the same

district. Such conditions as sanitation and the eating of fish, meat and flour can be excluded. Two factors remain, *viz.*: (1) The Bengalis take parboiled or steamed polished rice, while the Marwaris do not use rice at all or, if they do, only polished "atap" rice. (2) Marwaris do not use mustard oil for cooking, but only for preserving certain articles of food. Facts are given which suggest that mustard oil and parboiled or steamed rice may be causative factors. Nevertheless, the author quotes his own personal experience, which points to the presence of another unknown factor. He and other members of his family were attacked with epidemic dropsy in 1932. As soon as the first symptoms appeared they all left home, but took their food (including rice and mustard oil) with them. Most of them were cured in a few days, but as soon as the author returned home the disease recurred. The only changed factor in this instance was water. According to the author, rice and mustard oil prepare the soil, and microorganisms in water produce the actual disease.

The usual *post mortem* findings of the disease are described and under the heading of symptomatology the following may be noted:—Oedema of the legs and other parts is, of course, the chief symptom but serous effusions are rare. Palpitation and dyspnoea occur in about 50 per cent. of cases. Cardiac failure may be acute and rapidly progressive. In addition to the usual skin manifestations, pigmentation occurs in nearly all cases and the hair frequently falls out. Glaucoma is present in about 5 per cent. of cases and haemorrhoids are sometimes met with. If the patient be removed to a place free from the disease on the very first appearance of symptoms death is rare. 2 to 5 per cent. of sufferers die from heart failure.

There is no specific treatment and vitamin preparations have no effect. Removal of the patient from his former surroundings, omission of mustard oil and rice from the diet and boiling drinking water are the most successful measures. If it is impossible to exclude rice from the diet only the "atap" variety should be allowed.

A. D. Bigland.

MASSIAS (C.). Myosites suppurées observées en Cochinchine. [**Suppurative Myositis seen in Cochin-China.**]*—Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 768-770.

A brief account is given of ten cases in Annamites, in which the site of inflammation was the thigh muscles, buttocks, lumbar muscles, deltoid or calf, and of three cases in which more than one group was affected. All were treated by free incision and irrigation with a chlorine solution. Blood culture was never positive. In nearly all instances a staphylococcus was present. This organism plays a considerable part in Indo-China, where epidermitis, boils, abscesses of the scalp in children, pyuria, are frequent. Myositis is much less common. It can be explained only by a blood infection in persons with a staphylococcic skin lesion.

A. G. B.

HUARD (P.) & RENUCCI (N.). 33 observations de myosites. [**33 Observations of Myositis.**]*—Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Nov. Vol. 12. No. 9. pp. 825-860.

The 33 cases of myositis described case by case were staphylococcal in 26 instances, streptococcal in two, paratyphoid in one and in four

the nature was not determined. Treatment was chiefly by lavage with bacteriophage.

The senior author returns to this subject [23 observations were reviewed in this *Bulletin*, Vol. 30, p. 808]. What follows concerns the staphylococcal cases alone. Some diagnostic errors are discussed. Development was often acute, but sometimes sub-acute and "cold." Treatment, he says, has been transformed by bacteriophage. Almost invariably its injection is followed promptly by cessation of inflammation, and when absorption does not take place a small incision suffices for cure. The treatment must be applied exactly with no fault of technique. The focus of suppuration has to be determined, not always an easy task. When the trocar has entered the cavity it must be emptied completely, so that the trocar must not only be in the right place but be large enough to evacuate all the débris. Once empty the cavity is washed several times with bacteriophage and is then emptied entirely. Puncture plus lavage is renewed 2-4 times. The phage is rarely given by the veins and never under the skin. If a fistulous opening is present the phage is not used. After surgical cure orthopaedic treatment is often needed, followed by physiotherapy.

By this treatment serious complications are avoided and recovery is rapid. [The authors do not give the source of the phage or any detail beyond what is told here.] A. G. B.

MASSIAS (Charles). *Pathologie tropicale. La melioidose. [Melioidosis].*—Reprinted from *Gaz. des Hôpît.* 1934. Oct. 13. Vol. 107. No. 82. pp. 1449-1452. [33 refs.]

A very good account is given in this general review of melioidosis, its history, the clinical features of its acute, subacute and chronic manifestations, its diagnosis, the differential characters of its causal bacillus, and its epidemiology.

How protean in its appearance the disease may be is evident from the list of some of the diseases with which it has been compared or confused:—septicaemic plague, malignant malaria, cholera, typhoid fever, typhus, broncho-pneumonia, pulmonary abscess, galloping phthisis, abscess of the liver, pyelonephritis, osteitis and subcutaneous multiple abscess. Blood culture alone will provide the diagnosis in acute cases and pus culture is indispensable in chronic cases. The main pathological lesions are miliary granulations with necrotic centre in all organs. These may increase in size as the disease continues and appear as caseous foci and abscesses. A useful table is given of the common and differential characters of the bacillus of Whitmore and the glanders bacillus. Some of these may be given as:—

(1) *Common*:—gram-negative, aerobic, growing on ordinary media, brown pigment on glycerinated potato, and crossed fixation of complement reaction. (2) *Differential*, by pairs, for *Pf. whitmori* and *Pf. mallei* respectively:—motile and non-motile; cultures profuse and sparse; colonies rarely oily and none but oily; pellicle on broth abundant and absent; milk coagulated on the 4th day and the 10th day; gelatin liquefied and non-liquefied; highly and feebly pathogenic for rodents; feeble and very high pathogenicity for the equidae; cuti-reaction rarely positive to mallein and rarely positive to whitmorin.

Under epidemiology the views of STANTON and FLETCHER are accepted that rats suffer from epizootics and are probably the reservoirs

of the virus. Human infection is brought about by contamination of food with rat dejecta. W. F. Harvey.

JAMES (Clifford). Chronic Maxillary Sinusitis (Suspected and Un-suspected) in the Tropics.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 6. pp. 635–644. With 1 map & 1 chart. [11 refs.]

The author finds this condition common in that part of the tropics where his practice lies, the islands of Choiseul in the British Solomons and New Britain in the Mandated Territory of New Guinea, both with hot and moist climates. Among the 60 cases studied the diagnoses had been pulmonary tuberculosis, influenza, asthma, chronic bronchitis, chronic malaria, sarcoma of the maxilla, fibrositis; many of which were only complications.

The complications may be serious, including extension of inflammation to ear, eye, orbit and brain; by inhalation; by the sinus acting as a focus of infection, causing toxæmia and affection of joints or fibrous tissues. Of 30 complications mentioned in his paper, 18 occurred in his own cases. Once the condition is diagnosed treatment is effective. The chief symptoms in descending order of prevalence were headache, most severe in the morning and mostly frontal; chronic cough; fever; influenzal attacks caused by temporary blocking of the ostium of the sinus; asthma; fibrositis; ear complaints, either from extension or reflex; other symptoms were only occasional. There was almost always a nasal voice and sometimes a nasal discharge. For diagnosis he employed direct examination of the nose with or without cocaine and postural tests and puncture, each of which is described. Puncture was positive, *i.e.*, revealing excess of mucus or pus or muco-pus, when nasal examination was negative in one-third of the cases. There was no case of dental origin. Treatment is by wash-outs or radical operation. A. G. B.

ALLEN (F. R. W. K.). Five Cases of Rhinosporidiosis, Four in Females.—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 76–77.

It is interesting to note that of the five cases of rhinosporidiosis which are here placed on record, four were in females. The author considers that rhinosporidial infections may not be uncommon in rice-growing districts. "It is possible that the spores are inhaled when rice is being husked." Recurrences are common even after removal of the polypoidal nasal lesions unless great care is taken to remove all the tumour together with its pedicle. W. F. Harvey.

LATHAM (D. V.). Gillan's Oedema.—*East African Med. Jl.* 1935. Feb. Vol. 11. No. 11. pp. 358–360.

The author describes a case which he regards as "Gillan's oedema" [*ante*, page 71]. The patient was a girl of 4 years who had all the symptoms given by GILLAN and in addition a hookworm infection. She received calcium lactate and glucose and made a complete recovery. Afterwards the hookworms were banished by carbon tetrachloride but only after a third attempt.

The author believes this disease to be hitherto undescribed.

A. G. B.

AZMY (S.), GAAFAR (M.) & NOSHOKATI (H.). Observations on Anaemia in Egypt.—*Jl. Egyptian Med. Assoc.* 1934. Sept. Vol. 17. No. 9. pp. 739-754.

—, —, & —. **Observations on Anaemia in Egypt.**—*Jl. Trop. Med. & Hyg.* 1934. Oct. 15. Vol. 37. No. 20. pp. 311-316. With 1 chart.

These practically identical papers deal with 150 cases of hypochromic microcytic anaemia in Egypt, associated with ancylostoma in 24 cases, bilharzia 17, mixed 37, splenomegaly 8, pellagra with or without parasites 57, chronic dysentery 3, ascariis 2, achlorhydria without parasites 2.

Ancylostoma.—Severe, haemoglobin below 30 per cent. in 16 with lowest 10, red cells usually between 2 and 3 millions with lowest 1,120,000, corpuscular resistance and icteric index normal; of 18 cases 2 had achlorhydria and 6 hypochlorhydria; there were haemic murmurs, harsh and marked, not usually disappearing on treatment, with marked improvement in the anaemia.

Schistosomiasis.—Haemoglobin not less than 40 in urinary, not less than 25 in intestinal cases, the red cells being not less than 3 and 1.8 millions respectively, fragility and icteric index normal, hypoacidity commoner in intestinal infection.

Splenomegaly.—Haemoglobin not less than 45 and red cells than 3 millions, usually cured by iron without reduction in size of the spleen.

Pellagra: without parasites 12 who had haemoglobin above 55, red cells 4 millions or more, colour index usually below 1, gastric acid usually below normal. They improved rapidly, except for the nervous symptoms, on ordinary hospital diet.

Simple achlorhydric anaemia.—Reduced iron gave very good results, improvement being, however, somewhat more rapid when dilute hydrochloric acid was added.

In treatment the best results were obtained with reduced iron 2 grams thrice daily after food, combined with 2 to 8 cc. of [?] dilute hydrochloric acid in water. Liver increased slightly the red cell numbers but not the haemoglobin; arsenic diminished the latter; vitamins were of no particular value; blood transfusion was given in urgent cases, but unless followed at once by iron administration the temporary benefit was lost. Cases are cited to show the following:—Failure of a man with haemoglobin at 25 to benefit from deworming till iron was given, deleterious effect of arsenic on haemoglobin, cure of anaemia without expulsion of worms but "if administration of iron is stopped and the parasites are still present the anaemia recurs. That is why anthelmintics are essential."

Clayton Lane.

CAMERON (J. A. P.). Two Cases of Gout recorded with Commentary.—*Malayan Med. Jl.* 1934. Dec. Vol. 9. No. 4. pp. 206-208. With 2 figs.

1. A male Cantonese *aet.* 38, 20 years resident in Malaya, had history of pain and swelling in the joints for 3½ years. Tumours removed from the sole, dorsum of feet and trochanter, consisted of chalky matter and white creamy material found to be practically pure "acid urate" crystals. X-ray photo of knee joint showed osteo-arthritis lipping. The blood uric acid percentage was 6.37 mgm. as compared with the normal 1-3 mgm.

2. In the second case with an eight years' history the changes—disorganization of articulations with bony ankylosis—were those of rheumatoid arthritis and the blood uric acid was 5.45 mgm. per cent.

The Editor states that gout is "not uncommon" in Malaya: the etiology is obscure.

A. G. B.

CHOPRA (R. N.) & GHOSH (Sudhamoy). **Some Common Indigenous Remedies.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 263-270. [21 refs.]

The authors give a description of their studies on the chemical composition, pharmacological action and therapeutic properties of some of the common remedies used in Indian indigenous medicine. Since the result was to show that the quantities of physiologically active substances contained were insufficient to produce marked effects it will be sufficient to give a list:—

Picrorrhiza kurroa, Benth., N.O. Scrophulariaceae.

Erythrina indica, N.O. Leguminosae; the Indian coral tree.

Sansevieria zeylanica, N.O. Liliaceae; a fibre plant.

Pongamia glabra, N.O. Leguminosae.

Hygrophila spinosa, N.O. Acanthaceae.

Bryophyllum calycinum, Salisb. N.O. Crassulaceae.

Rheum emodi, N.O. Polygonaceae; one of the rhubarbs.

Solanum indicum, N.O. Solanaceae.

A. G. B.

KENNEDY (Walter P.). **The Polynuclear Count in an Iraq Population.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 475-480. With 3 figs.

The author starts by a brief exposition of the Arneth count and refers to the work of W. E. COOKE who together with E. H. PONDER has probably done more work on this subject than anyone else. He then gives the average count and index for Britain and states that it is "more useful to express the result as a single index, and for this purpose the weighted mean gives a very sensitive measure of the state of the count. The average weighted mean of the above series [of COOKE and PONDER] is 2.74 with a standard deviation of 0.18," but unfortunately for the average reader he does not define the term "average weighted mean." Most people are agreed that infection usually [but not always] brings about a shift to the left and in order to interpret what constitutes a shift to the left it is essential to know what are the normal limits for the district in which the test is made. It certainly differs in the tropics from what obtains in temperate climates, and, moreover, the reviewer, when studying this question 20 years ago, found that there were differences between the white man and the native in the same country. BREINL and PRIESTLEY have shown that the index differs between native adults and children in New Guinea [see this *Bulletin*, 1916, Vol. 7, p. 336].

As a preliminary to possible work in the future the author has examined 121 samples from inhabitants of Iraq to establish as near as he can the normal in that country. He took them from three representative groups: Kurds from Kirkuk, Dulaimi from Haditha, and Jews from Sandur, and found a decided shift to the left as compared with British figures. Though there are several infections not severe enough to prevent a man working and such a man when asked if he was in good health would reply in the affirmative, the author

does not accept these cryptic infections as the sole cause of the difference in the count. "The possible influence of environmental factors is a question requiring further investigation." In the tropics certainly and, it may be, in other places also the possible disturbing factors rob the Arneth count of much of its reputed value as an indicator of morbid conditions. *H. H. S.*

CATANEI (A.). Recherches parasitologiques et expérimentales sur la sporotrichose, les blastomycoses et l'actinomycose, en Algérie. [Parasitological and Experimental Researches on Sporotrichosis, Blastomycoses and Actinomycosis in Algeria.]—*Arch. Inst. Pasteur d'Algérie*. 1934. Sept. Vol. 12. No. 3. pp. 351-366. With 3 text figs. & 6 figs. on 1 plate.

This is an account of some fungi isolated, in Algeria, from human disease and from water. The clinical features and morbid anatomy are not given.

(1) *Sporotrichosis*.—A culture of *Rhinocladium Beurmanni* was recovered from a nodular sporotrichosis of the lower limb. It had little or no pathogenicity for white mice, and it agreed with the descriptions by DE BEURMANN and GOUGEROT of the French strains of this species.

A fungus, identified as *Sporotrichum biparasiticum* Bubak, was cultivated from a sample of well water. Descriptions of its growth characters and spore measurements are given. It proved to be pathogenic for mice and other animals by inoculation, subcutaneously or intravenously, and showed much greater virulence than the culture of *R. Beurmanni*. Subcutaneous inoculation gave rise to a gumma which broke down after about eight weeks and discharged on the surface; cure followed and there was no tendency towards a generalized infection. Intraperitoneal inoculation into rabbits, mice or new-born guineapigs caused a peritoneal sporotrichosis, sometimes with foci in the spleen and liver, and death. The fungus appeared in the lesions usually as masses of tangled filaments with rounded or oval elements 2.5 μ to 4.5 μ in diameter. The fungus could be cultivated from the pus or lesions but attempts to transmit the infection from animal to animal by inoculation of morbid material failed, except in one instance when a local lesion resulted.

The serum of infected animals contained no demonstrable antibody and, after recovery, the animal was susceptible to reinfection.

(2) *Blastomycosis*.—Two "new" fungi are described. The first, a yeast fungus belonging to the genus *Candida* Berkhout, was isolated from blastomycosis of the forearm. A description is given of the growth characters on various media, fermentations, etc., and the fungus has been named *Candida Montpellicieri* n. sp. The description leaves the reviewer in doubt as to the justification for placing the fungus in the genus *Candida*, and a similar doubt may have affected the authors for they named it at first "*Cryptococcus*." The identity cannot be confirmed as the culture has been lost.

Intravenous injection of large quantities of the culture into a rabbit was without apparent effect, but subcutaneous inoculation caused a local gumma which later broke down and discharged. Cultures recovered from the animals were not more virulent than the parent culture. Intravenous inoculation evoked a high titre of agglutinin in a rabbit's blood but did not protect the animal against the effects of

subcutaneous inoculation. The agglutinating serum had no effect on "*Monilia albicans*."

The second fungus from Blastomycosis was isolated from a lesion of the lower extremity. It appeared in the tissues as bodies 4.0 μ to 10.0 μ by 2.0 μ to 6.0 μ , grouped in little masses or in short chains, usually in close relation to giant cells. The fungal elements were brownish and unstainable. A culture was obtained by puncturing an unbroken gumma, and the fungus was identified as a *Hormodendron* Bonorden 1857, and was named *Hormodendron algeriensis* n. sp.

Subcutaneous inoculation, into a rabbit, of a culture in hay infusion caused a voluminous abscess, but no generalization followed. Pigeons and mice were apparently resistant.

(3) *Actinomycosis*.—There were three cases of actinomycosis, two affecting the face and one pleuropneumonic. The "grains" were greyish-white, about 0.5 mm. in diameter, soft and irregular in shape, they were made up of slender mycelial filaments about 1.0 μ in diameter, Gram positive but not acid fast. Only the grains from the lung showed club-formations. Culture, in all cases, yielded the same species of actinomycetes, the anaerobic *Cohnistreptothrix israeli* Kruse 1896. Animal inoculation with the cultures or "grains" gave negative results.

J. T. Duncan.

SHREWSBURY (J. F. D.). **The Genus *Monilia***.—*Jl. Path. & Bact.* 1934. May. Vol. 38. No. 3. pp. 313-354. With 32 figs. on 9 plates. [27 refs.]

This article gives an account of a careful study of various species of fungi which have been assigned to the genus *Monilia*. The author describes the morphology characteristic of the type and some of the departures from it which several of the species present. He next considers the staining reactions, cultural characters on solid and liquid media, biochemical properties in relation to action on litmus milk, their proteolytic and saccharolytic powers and general fermentative action, and ends with a discussion as to which of the species examined belong strictly to the genus. Those investigated were Mackey's "*M.*" *Monilia psilosis*, *M. albicans*, *M. candida*, *M. krusei*, *M. pinoyi*, *M. tropicalis*, and Marrett's "*M.*" It is shown that some at least of these, *M. krusei* Cast. for example, have no right to a place in the genus. It will be seen that the paper is largely a systematic study and a most praiseworthy attempt to bring order out of the chaos into which this, at present, somewhat arbitrary group has fallen.

H. H. S.

SALAH (M.). **Sternal Puncture. (A Preliminary Note.)**—*Jl. Egyptian Med. Assoc.* 1934. Oct. Vol. 17. No. 10. pp. 846-850. With 1 fig.

The author uses for sternal puncture a lumbar puncture needle made of hard steel which with its stilet is cut to 3 cm. length. A moveable shield fits round the needle with a screw to fix it at the required distance [cf. KASSIRSKY, this *Bulletin*, Vol. 31, p. 658]. This varies from 0.4 to 1.0 cm. according to age and size of patient. The middle of the sternum opposite the third space is the best place for puncture. No incision and no local anaesthesia are needed. He discusses the value of puncture in the diagnosis of anaemias and splenomegalies. He has used the method in a series of 92 cases without untoward effect.

A. G. B.

BRUMPT (E.). Au sujet des changements de propriétés biologiques des germes chez divers hôtes vecteurs vicariants. [**Changes of Biological Properties of Microbes in Different Vector Hosts.**]*—Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 830-831.

The text of Brumpt's paper was the failure of an attempt by LE CHUITON and BOURGAIN to convert a strain of murine typhus into boutonneuse fever by passage through *Rhipicephalus sanguineus*; they were unable to transmit the strain by the progeny of the tick. Brumpt points out that intermediate hosts whether normal or vicarious do not seem to modify the biological properties of germs which they transmit. Thus, *Spirochaeta duttoni* has the same characters whether it is transmitted by *O. moubata* as in Central Africa or by *O. erraticus* as in Dakar, whereas *S. hispanica* though likewise transmitted by *O. erraticus* has retained its peculiar characters, such as its pathogenicity for the guinea-pig. The virus of exanthematic typhus which has developed in fleas is not transformed into murine typhus and that of Rocky Mountain fever transmitted from louse to louse for a period of 5 months also keeps its own characters. *Trypanosoma cruzi* is equally virulent whether transmitted by Triatoma, Rhodnius or *O. moubata*. For this reason Brumpt cannot admit the unicity hypotheses of those who think that the various forms of typhus are all due to one virus which is transformed in passage through louse, flea, tick or mite or of those who suppose that *T. rhodesiense* loses some of its virulence and becomes *T. gambiense* by a change of vector to *G. palpalis*.

A. G. B.

ANDERSON (Nelson Paul) & AYRES (Samuel), Jr. **Light Sensitive Dermatoses.***—Jl. Amer. Med. Assoc.* 1934. Oct. 27. Vol. 103. No. 17. pp. 1279-1285. With 7 figs. [41 refs.]

There is reason to believe that disturbed sulphur metabolism plays a part in the production of light dermatoses. It has been shown, for example, that the lethal action of ultra-violet light on paramoecia is diminished by the interposition of a solution of cystin, an amino-acid containing sulphur. It is notable, too, that the protective epithelial tissues, such as skin, hair and nails, contain a greater sulphur content than do other tissues.

Haematoporphyrin has a powerful light sensitizing power when injected experimentally. But it has not been shown that it is an underlying cause of light sensitivity; indeed it has only been found in the urine of a small proportion of cases of hydroa aestivale, and further porphyrin in the urine has been found in many cases which were not light-sensitive; nor was it present in the authors' cases of light sensitivity; in these cases no other photo-dynamic substances could be found in the urine.

The irritative effect of sunlight on lupus erythematosus is well known, for it often follows severe sunburn. An account is given of a dietetic treatment of that condition but the cause of its effectiveness is not known. Various drugs, including eosin, acriflavine and methylene blue are light sensitizers; their usefulness in therapeutics is problematical. Sunlight is a factor in the production of many cases of vitiligo and light plays a part in the production of the skin lesions of pellagra, although light is not the only factor involved. Fagopyrism

is a disease occurring only in lightly pigmented cattle which have ingested buckwheat, which contains a light sensitizing substance.

Some figures illustrate the effects of treatment in some dermatoses.

R. G. Bannerman.

- CHOPRA (R. N.), GHOSH (Sudhamoy) & DUTT (Ashutosh). Some Inorganic Preparations of Indian Indigenous Medicine. Part I. *Abhra Bhasma*.—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 285-288.
- CLEMENTS (F. W.). The Relation of Diet to Tropical Ulcer: a Preliminary Report.—*Med. Jl. Australia.* 1934. Apr. 21. 21st Year. Vol. 1. No. 16. pp. 520-522.
- CORMACK (R. P.). Some Subjects for Medical Research in East Africa.—*East African Med. Jl.* 1934. Dec. Vol. 11. No. 9. pp. 276-285.
A paper worth perusal but unsuitable for summary.
- DEVASAGAYAM (A.). Notes on Some Intestinal Affections of Tamil Coolies.—*Malayan Med. Jl.* 1934. Dec. Vol. 9. No. 4. pp. 200-204.
- DONATELLI (Leonardo). Ricerche farmacologiche sull'olio di chenopodio. Nota seconda.—*Pediatrics.* 1935. Feb. 1. Vol. 43. No. 2. pp. 161-176. With 16 figs. English summary (6 lines).
- GORGAS MEMORIAL INSTITUTE. Annual Report of the Gorgas Memorial Institute, 1933 [GRAYSON (Cary T.), MARTIN (Franklin) & CLARK (Herbert C.)]. 73rd Congress. 2nd Session. Document No. 205. House of Representatives. 8 pp.
- KIKUTH (Walther). Neue Wege in der Behandlung der Tropenkrankheiten.—*Klin. Woch.* 1934. Nov. 10. Vol. 13. No. 45. pp. 1593-1595.
- KITABATAKE (Eitaro). Parasitic Diseases among Immigrants in Aikawa Village, Kinshu and in Denshodai Farm, Eiko, Manchoukuo.—*Jl. Oriental Med.* 1935. Feb. Vol. 22. No. 2. [In Japanese pp. 369-377. With 2 figs. English summary p. 32.]
- KOUWENAAR (W.), MAASLAND (J. H.) & WOLFF (J. W.). Onderzoekingen over het rhinosclerom op Sumatra.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Sept. 11. Vol. 74. No. 19. pp. 1187-1200. With 1 map & 8 figs. on 4 plates.
- KOUWENAAR (W.), MAASLAND (J. H.) & WOLFF (J. W.). Onderzoekingen over het rhinosclerom op Sumatra.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Nov. 6. Vol. 74. No. 23. pp. 1494-1513. With 1 plate. [30 refs.] English summary.
- LEASE (Jane Germer) & PARSONS (Helen Tracy). The Relationship of Dermatitis in Chicks to Lack of Vitamin B₂ and to Dietary Egg-White.—*Biochem. Jl.* 1934. Vol. 28. No. 6. pp. 2109-2115. With 1 text fig. & 4 figs. on 1 plate. [24 refs.]
- DE LEON (W.), DE JESUS (P. I.) & RAMOS (J. M.). Weights of Visceral Organs of Filipinos in Different Diseases.—*Philippine Jl. Sci.* 1934. Aug. Vol. 54. No. 4. pp. 495-522.
- VAN LOON (J. Potter). Een geographisch-pathologische bijdrage tot het galsteenvraagstuk. Onderzoek met de duodenumsonde bij Javanen en Chinezen.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1934. Dec. 25. Vol. 74. No. 26. pp. 1736-1748. With 2 figs. [34 refs.]
- MANSON-BAHR (P.). Whither Tropical Medicine? An Epitome of Scientific Activities in British Tropical Possessions, together with a Consideration of the Position which Tropical Medicine occupies in Scientific Medicine at the Present Time.—*Proc. Roy. Soc. Med.* 1934. Nov. Vol. 28. No. 1. pp. 57-66 (Sect. Trop. Dis. & Parasit. pp. 1-10).
- O'CONNOR (F. W.). Concern of the United States with Tropical Diseases.—*Amer. Jl. Pub. Health.* 1935. Jan. Vol. 25. No. 1. pp. 1-10.
- PEIRIER (J. C.). Matières colorantes injectables.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Aug.-Sept. Vol. 12. No. 7. pp. 704-719. With 5 charts.

- PRICE (A. Grenfell). The White Man in the Tropics.—*Med. Jl. Australia*. 1935. Jan. 26. 22nd Year. Vol. 1. No. 4. pp. 106–110.
- SCHWARZ (Joseph L.). The Practice of Medicine in American Samoa.—*U.S. Nav. Med. Bull.* 1935. Jan. Vol. 33. No. 1. pp. 27–35. With 3 figs. on 2 plates.
An account of surgical practice.
- STEUDEL (F.). Die Seuchenbekämpfung in Deutsch-Ostafrika.—*Med. Welt*. 1934. Nos. 39 & 41. 18 pp.
- UHLENHUTH (P.). Neue Fortschritte auf dem Gebiet der Antimonbehandlung von Tropenkrankheiten.—Reprinted from *Therap. d. Gegenwart*. 1934. No. 10. 6 pp.
- VON WIKULLIL (L.). Badgastein in the Treatment of Tropical Diseases.—*Jl. Trop. Med. & Hyg.* 1935. Mar. 15. Vol. 38. No. 6. pp. 74–76.
- ZIEMANN (Hans). Neuere aus dem Gebiete der Infektionskrankheiten der exotischen Pathologie, Parasitologie und Hygiene.—*Med. Klin.* 1935. Jan. 25. Feb. 1 & 8. Vol. 31. Nos. 4, 5 & 6. pp. 121–124; 153–154; 186–188.

REVIEWS AND NOTICES.

REDAELLI (P.); BASERGA (A.); GIORDANO (A.); SORGE (G.); PARADISO (F.) & FIORENTINO (A.); ZANGRI (G.); PIAZZA (G.). **Ricerche e studi sulla leishmaniosi viscerale del Mediterraneo.** [Studies on Visceral Leishmaniasis of the Mediterranean.]—191 pp. With 7 plates (2 coloured) & 1 text fig. 1933. Catania: Società Medico-Chirurgica di Catania. [Lira 30.]

The publication contains a series of eight articles by various authors on canine and infantile kala azar as it occurs in Catania. The first and most comprehensive of these is a detailed study of the pathology of canine kala azar based largely on naturally infected dogs which had been taken to Catania from Malta by ADLER for the purpose of sandfly feeding experiments. The information given is mainly confirmatory of previous work. It is worthy of note, however, that apart from the well known generalized distribution of leishmania throughout the internal organs in histiocytes the parasites occur fairly uniformly in these cells in all parts of the skin, even in animals showing no visible skin changes, and also in the mucosa of the nose, mouth and oesophagus, as well as in that of the entire intestinal tract. In the second article attention is drawn to the changes in the bone marrow of infected dogs, while in the third emphasis is laid on the fact that occasionally parasites occur in megacaryocytes. The fourth article records the experimental infection of the spermophile (*Citellus citellus*) with a canine strain of the kala azar parasite and gives some details of the histopathology of the infection in this animal. The fifth article is a review of recent work on the subject of sandfly transmission of kala azar, while the last three are devoted to a consideration of the infantile disease, particularly the success of intramuscular treatment with neostibosan and fuadin and the more prolonged rate of excretion of antimony when the organic compounds are given intramuscularly, a method of administration which appears to reduce the toxic effects by forming deposits from which the drug is slowly absorbed.

C. M. Wenyon.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 8.]

LEPROSY.

MCKINLEY (Earl B.). **The Etiology of Leprosy.**—Reprinted from *Medicine*. 1934. Dec. Vol. 13. No. 4. pp. 377-504. With 12 figs. [525 refs.]

This is in itself a comprehensive review of the bacteriology of leprosy for the past sixty years with 525 references, which should be read by all interested. The author concludes that there is still no absolute proof that Hansen's bacillus is the cause of leprosy, although no one doubts it, for it is not generally accepted that organism has been cultivated, nor has typical leprosy as seen in man been reproduced in lower animals. He is hopeful that his tissue cultures may yet prove successful, and the work of REENSTIERN, himself and others on inoculation of monkeys is promising. Similarly the chemistry of the lepra organism is also much more deficient than that of the tubercle bacillus.

L. Rogers.

- i. NOLASCO (J. O.). *Mycobacterium leprae* in Deep Organs in Fifteen "Quiescent" and "Arrested" Cases of Leprosy not demonstrated in Smears at Necropsy.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 705-713.
- ii. HUIZENGA (Lee S.). **The Application of Sterilization in Leprosy.**—*Ibid.* pp. 783-790.
- iii. HOANG-PHO. Un cas de paralysie générale d'origine lepreuse. [G.P.I. of Leprotic Origin.]—*Ibid.* pp. 721-723.
- iv. LAI (Daniel G.). **A Bacteriological Study of Certain Immune Regions in Skin Leprosy.**—*Ibid.* pp. 725-727.
- v. REISS (F.). **Tuberculoid Leprosy, a Clinical Entity or a Histopathological Reaction.**—*Ibid.* pp. 699-704. With 6 figs. on 3 plates.

Of the 12 papers in this volume seven, noted by title only on pp. 554 & 555, relate to work of the same writers that has already been reviewed in this *Bulletin*. The following are the main points in the remaining papers.

i. J. O. NOLASCO in continuation of previous work reports on the post-mortem examination for lepra bacilli in the tissues of 15 more "arrested" cases of leprosy. The organisms were not found by direct smears, but in 12 of them histological examinations showed the micro-organisms associated with typical foamy cells; in the remaining three the infection was

considered to be overcome, and in others the bacilli were believed to be undergoing intracellular digestion within the foamy cells, so they may have been dead. The importance of a follow up of paroled cases is emphasized.

ii. L. S. HUIZENGA reports on the presence of anhydrosis and alopecia in 200 lepers. They are nearly always found in active cases, and are attributed to destruction of the glands and the nerve ends by pressure of leprosy infiltration. The face and extremities are most affected, but the general health does not suffer much.

iii. HOANG-PHO reports a case of general paralysis in a leper in whom he was unable to find evidence of syphilitic infection.

iv. Daniel G. LAI has made a bacteriological examination of the skin of certain regions reported by HOPKINS to be usually immune to evident leprosy lesions, and in an examination of 83 cases he found that leprosy bacilli were commonly present in small numbers as compared with adjacent infiltrated areas of the skin.

v. F. REISS has given, in addition to chaulmoogra preparations, sodium thiosulphate, which PALDROCK and POOMAN had found to have some action on leprosy bacilli. He reports on seven cases, five of which showed marked and rapid improvement on the combined treatment, which he therefore suggests may be found by further work to be of value.

L. R.

LEPROSY REVIEW. 1935. Jan. Vol. 6. No. 1. pp. 1-49. With 12 figs. (1 map) on 4 plates.—Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W. 1. [2s.]

In this number G. R. RAO reports a trial of brilliant green, trypan blue and Bonney's blue in 20 leprosy cases at Purulia with no appreciable effect on either the course of the disease or on the leprosy bacilli.

Gordon A. RYRIE writes on the management of reactions following either over dosage or abrupt cessation of prolonged hydriodone treatment; concurrent disease such as syphilis, sepsis or helminthic infections; or possibly such foods as shell-fish, curries, etc.; drugs such as KI; or emotional stress. Cessation of hydriodone treatment for a full month after subsidence of the reaction is advised. Further comments on Dr. ROSE's article [*ante*, p. 328] and reprints of papers already dealt with in this *Bulletin* are included.

L. R.

LEPROSY REVIEW. 1935. Apr. Vol. 6. No. 2. pp. 51-99. With 7 figs. (5 on 2 plates), 1 plan & 1 map.—Quarterly Publication of the British Empire Leprosy Relief Association, 131 Baker Street, London, W. 1. [2s.]

The first paper in this number is a valuable description of the well-known methods of examining leprosy lesions for the causative bacillus for diagnostic purposes by that very experienced pathologist, H. W. WADE, which should be read in the original by those interested.

Spencer B. MCNAIR contributes a review of eye, ear, nose and throat work at the Carville Leprosarium, which is fortunate in having a specialist staff. A number of operations have been performed for the relief of ectropion. The electric cautery is advised in the treatment

of infiltrated areas about the limbus of the eye and ulcerated areas in the larynx. Corneal infiltration and iridocyclitis are major eye problems for which he advises atropine twice daily, salicylates for pain, and subcutaneous or intramuscular injections of foreign protein in the form of diphtheria antitoxin, haemoprotein of Brooks or a milk preparation, aolin. In chronic keratitis gold sodium thiosulphate intravenously, foreign proteins and instillations of 20 per cent. chaulmoogra oil and dionine into the conjunctival sac are recommended. The electric cautery is used in leprosy lesions of the nose, followed by spraying 30 per cent. chaulmoogra oil in olive oil or chloretone inhalant. For stenosis the affected turbinate bone is removed. Tonsillectomy has frequently been performed. Tracheotomy may be required for laryngeal obstruction. Ear lesions are limited to the external portions.

R. G. COCHRANE commences in this number an account of his recent tour in the West Indies. In Jamaica under the Leper Asylum Law of 1896 pauper and indigent lepers were segregated and others were allowed to live at home under certain restrictions. The number in the asylum has averaged about 120 in spite of an increasing population; so he thinks the disease is diminishing, but the law may require modification and endemic foci should be sought for and the infected dealt with in leper colonies with land to cultivate. A special medical officer should be sent to the Trinidad Leper Settlement for study so as to be able to recognize early cases.

Barbados has compulsory segregation, but the numbers isolated have fallen during the decade 1924-34 from 173 to 75, and 55 more discharged cases receive monthly allowances and are prohibited from certain forms of work. The asylum is prison-like and requires ground around it. From the admission records the distribution appears to be patchy and surveys are needed to find and deal with the foci of infection to hasten the disappearance of the disease from the island.

The remaining papers are reprints, including the report on the Uganda settlement which appeared in the *East African Medical Journal*. (Ante, p. 331.)

L. R.

LIE (H. P.). **The Curability of Leprosy.**—*Internat. Jl. Leprosy*. Manila. 1935. Jan.-Mar. Vol. 3. No. 1. pp. 1-22. With 8 figs. on 2 plates. [12 refs.]

This interesting historical paper on the treatment of leprosy in Norway, from the time that DANIELSEN commenced work at the Bergen Hospital in 1839, brings out the foresight of that great worker in advocating attention to the patient's general health, the use of counter-irritants, a gold preparation, the production of reactions by potassium iodide, which he eventually recognized as harmful, and the use of *Ol. gynocardiae*—as chaulmoogra oil was then erroneously termed. Dr. Lie also records that a number of patients were found to be cured and free from lepra bacilli at later autopsies, and he emphasizes the tendency of the infection to die out in oldstanding cases, although this was infrequent, in 8 per cent. only in nodular cases. He also points out that "nodular patients who appear incapable of overcoming the bacilli may be completely cured when, for whatever reason, they are made to react. Here lies the most important problem regarding the therapy of leprosy, namely to bring about a reaction at as early a stage as possible."

L. R.

COCHRANE (R. G.). **The Epidemiology and Prevention of Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 385-394.

In view of the increasing number of early cases of leprosy now seen, and the tendency of many of them to abort if the patients, mainly children, are kept under good conditions, the author thinks such may be watched without treatment, which should be reserved for active cases, together with isolation in an institution, or in huts in the patients' villages, of infectious cases. This will simplify prophylaxis, in which propaganda should play an important part. The analogies between leprosy and tuberculosis are also stressed. L. R.

ATKEY (O. F. H.). **Leprosy Control in the Southern Sudan. A Compilation from the Annual Reports for 1929, 1930 and 1931 on the Medical and Health Work in the Sudan.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.-Mar. Vol. 3. No. 1. pp. 73-79.

This article has been compiled from official reports that have already been dealt with in this *Bulletin*. The conclusions are come to that many early cutaneous cases remain stationary and do not require segregation, but that measure is very beneficial in highly infective cases. Treatment certainly tends to keep the disease from advancing, though not spectacularly curative; improvement in food and conditions of living are most important measures. Bush dispensaries and providing treatment near the patients, with a central camp for highly infective lepers, are of value. L. R.

HOLLENBECK (H. S.). **Leprosy in Angola.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 6. pp. 655-656.

Leprosy is widespread in Portuguese West Africa, mainly in the nerve form, and appears to have increased on the plateau in recent years following deficient nourishment in partial famine years due to deficient rainfall. In 1925 the American Mission to Lepers supplied chaulmoogra oil for treatment in small colonies and camps with striking success from the first, for all the patients showed marked improvement in a few months; the early ones were discharged symptom-free in 18 months, and there were no relapses in those kept under observation for 9 years. In some more advanced cases 2 to 3 years' treatment produced steady improvement, and all but two became symptom-free, nodular cases responding about as well as nerve cases. The treatment is so popular that a large proportion could be treated if funds were sufficient. L. R.

GOURVIL (E.). **La lèpre au Soudan. [Leprosy in the French Sudan.]**—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 7-10.

Among 19,263 young men examined during recruitment in the French Sudan 401, or 20.8 per mille, were found to be infected. In 1928 under compulsory segregation 30 lepers were isolated, but general hiding of cases occurred and the results were "deplorable." Voluntary home treatment was then sanctioned and in three years there were 31 in the lazaret, but 271 enrolled for treatment with freedom. Indisputable amelioration was obtained in a large number by means of intravenous injections of emulsions of chaulmoogra oil, together with

general treatment with Fowler's arsenical solution and codliver oil, a combination superior to the first oil alone. Marriage of lepers with healthy persons, and certain dangerous employments are forbidden. Obedience to the rules and assiduous attendance for treatment surpassed expectations. L. R.

i. STRACHAN (P. D.). **Leprosy and Leprosy Treatment in Basutoland.**—*Internat. Jl. Leprosy*. Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 431-439.

ii. DYKE (H. W.). **Leprosy in the Bechuanaland Protectorate.**—*Ibid.* pp. 441-442.

iii. JAMISON (R.). **A Note on Leprosy in Swaziland.**—*Ibid.* p. 443.

i. In Basutoland the lepers are isolated in the Maseru asylum with about 600 patients and 1,500 acres of land, and with a convalescent village of 40 to 50 discharged cases. With greater activity the patients have increased recently to 730, and fewer very advanced ones are now admitted. Intradermal injections are readily accepted, but many cases have become arrested without active treatment, which has been very variable in degree, so analysis is difficult. The present isolation policy is very expensive.

ii. This brief note records that in dry Bechuanaland (200,000) only 25 lepers have been seen in five years and the number is estimated at 40 to 50, or 0.2 per mille. They are so scattered that regular treatment has not proved to be practicable.

iii. In Swaziland (125,000) the incidence is also low with not more than 120 cases, or about 1 per mille. Local isolation in huts is now attempted and nearly all the cases are of the nerve type, for the author has only seen two nodular cases in many years' work. L. R.

DEL TORO CANO (Fernando). El problema de la lepra en Marruecos occidental español. [**Leprosy in Spanish Morocco.**]—*Medicina Paises Calidos*. Madrid. 1935. Feb. Vol. 8. No. 2. pp. 85-103. With 1 map, 10 figs. & 1 chart. [22 refs.]

Twenty cases are referred to in this article, 9 of the nodular type, one macular, two mixed, and eight others are mentioned but not the type. The proportion is said to be 1 per 14,000 population in Western Morocco, or half as many again as in Spain (1 in 25,000). The nodular type is said to predominate. The disease is indigenous and not imported from Spain but some are said to have contracted their infection in the French territory. Before adequate prophylaxis can be effected a leper census should be taken and a leprosarium ought to be established for dealing with patients found, and immigration of lepers from other nations should be prohibited. There is a map showing the districts affected; of the 20 cases four were in Ceuta, five (a sixth doubtful) in Tetuán, two each from Jolot, Beni Manzor and Guezaua, and one each from four other districts. H. H. S.

MUIR (E.) & CHATTERJI (K. R.). **The Record of a Leprous Village with a Scheme for a Statistical Survey.**—*Leprosy in India*. 1935. Jan. Vol. 7. No. 1. pp. 4-18. With 1 fig. & 1 map.

This is an important record of a careful survey of a leprous Muslim Bengal village. It gives two family trees showing five generations, in both of which the disease began in the third generation, since

which 13 infective and 5 uninfected cases have occurred in one family, and 2 and 3 respectively in the other. A plan of the house infections is also given. Of the 23 cases in 46 years 19 survive, including 10 infective ones, who are now all isolated voluntarily in the village. The spread of the disease was apparently due to family relationship and closeness of residence, no less than 15 of the patients having probably been infected by one case. There is usually an average period of 6 years between the appearance of the first symptoms and the development of an infective stage, but, omitting one case, the average time was $3\frac{1}{2}$ years. The value of such a careful survey, with resulting voluntary isolation of all the infective cases is obvious, and schedules are given to assist surveys. L. R.

- i. SANTRA (I.). **A Note on Leprosy Work in the Salem District.**—*Leprosy in India*. 1935. Jan. Vol. 7. No. 1. pp. 23-25.
- ii. ——. **Notes on Leprosy in Japan.**—*Ibid.* pp. 26-32.

i. This brief note records the progress of widespread dispensary treatment in the Salem District of Madras. The author concludes that "treatment alone has a very great value in the control of the disease" and should not be discouraged by those who advocate segregation measures.

ii. This is a brief description of Japanese leper institutions seen during a short visit to the country. L. R.

KANG (T. I.) & WILSON (R. M.). **Statistical Data of 709 Korean Cases of Leprosy.**—*Internat. Jl. Leprosy*. Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 447-451.

An analysis showed 59 per cent. males and 41 per cent. females. In 30.3 per cent. the patients had lived with other lepers, brothers being the most frequent relationship. The disease was contracted in the first decade of life in 11 per cent., in the second in no less than 52 and in the third in 25 per cent., leaving only 12 per cent. over the age of 30 years. Poverty and deficiency of protein in the diet predisposed. Neural cases were 45, cutaneous 45 and mixed 11 per cent. Treatment was by chaulmoogra oil intramuscularly, with an average of 64 injections per case in 1933, with the result that 44 per cent. were arrested without deformities, and 42 per cent. more with deformities, with about equally good results in nerve and cutaneous cases, so the "results of treatment are encouraging." L. R.

LEE (H. S.). **The Statistical Observation of the Leprosy at Taiku Leper Hospital.**—*Japanese Jl. Dermat. & Urol.* 1934. Dec. Vol. 36. No. 6. [In Japanese pp. 651-657. English summary p. 113.]

Among 450 cases seen at Taiku, Korea, 427 were classed as early, with disturbance of sensation in 86.7 per cent., anhydrosis in 18.7, pemphigus in 32.8 and depigmentation in 21.7 per cent. The lesions were mostly found where mechanical pressure occurs frequently, and the patients mainly between the ages of 12 and 20 years, the disease beginning in the spring and affecting farmers most. L. R.

WAYSON (N. E.) & RHEA (Theodore). **Leprosy. Observations on its Epidemiology in Hawaii.**—*Public Health Bull. No. 212.* Wash. 1934. Sept. 32 pp. With 7 figs. [15 refs.]

This is an interesting statistical study of the incidence of leprosy in the Hawaii Islands, with tables and charts of data since they were more accurately kept from 1890.

After a brief discussion of the history of the disease, data are given regarding the variations in the mixed population, which show a decrease of pure Hawaiians and increase of half-breeds. The incidence of the disease shows a steady decrease in the admission rates during the last five decades, from 3.6 per mille in 1890–1900 to 1.3 per mille in 1920–30, especially among the younger ages; this is attributed to, or coincident with, “general biological and environmental influences which are evidenced by falling death rates from other causes, rather than as a result of specific control measures.” No evidence of definite racial susceptibility was found, and the sex ratio was 1 female to 1½ males, although up to the eighth year the ratios are practically equal, and the later excess in males is unexplained. Children under 15 are more frequently affected than older ones, especially in families with more than one case. Adolescence and pregnancy favour its development. Family incidence showed 3 or more cases in 10 per cent. and 2 or more in 30 per cent. of households. Among 420 families there were 600 admissions, or 20 per cent. of the total members, and 43 per cent. came from 14 families. Among a number of admissions between the ages of 10 and 15 the leprous condition had often been recognized three or more years before admission. The period of incubation could not be ascertained, and it is probably influenced by the degree of exposure to infection, for leprosy appears to be highly communicable under certain conditions. Poverty and diet deficient in animal proteins predispose, for the disease was most prevalent in rural conditions among families who had no milk or butter and inadequate vegetables and fruits, while calcium and vitamins B and C were also deficient.

L. R.

MACLEOD (J. M. H.). **Leprosy in Great Britain. The St. Giles Homes for British Lepers.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 67–70. With 3 figs. on 1 plate.

This is a very brief account of the St. Giles homes for British lepers. At a guess there are from 50 to 100 cases in Great Britain, almost all contracted in some part of the Empire abroad. The home was started in 1913 in a remote part of a home county by adding to farm buildings, and it is usually fully occupied by 12 male and 2 female lepers.

L. R.

COCHRANE (R. G.). **Leprosy in England.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 71–72.

This brief note is on similar lines to the above, but mentions that although infections are rare in this country the author has heard of three and possibly a fourth, but he “subscribes to the general view that conditions in England do not tend to cause the spread of leprosy.” The latent period may sometimes extend to a number of years, and

cases are often overlooked by medical men in this country for want of clinical experience until they have reached the second or third stage of the disease, when the prognosis is poor.

L. R.

MUIR (E.). **The Relationship of Skin and Nerve Leprosy.**—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 383-392.

This is a histological study of early lesions with a view to elucidating the relations of skin and nerve lesions, from which the following conclusions are drawn.

The infection spreads along the vascular plexuses of the sub-papillary and subcutaneous tissues up to the cutaneous nerve branches from the skin, the extension of the disease being lessened by natural and acquired resistance and favoured by any form of lowered resistance. The degree of cellular response is in proportion to the number of lepra bacilli in the tissues, with more rapid spread in young children and debilitated subjects, and less in older subjects with greater resisting powers, in whom it may cease to progress as long as the general health is good. The dermal nerves may show the highest number of bacilli owing to the lower resistance of nerve tissues. As subliminal infections increase immunity it is suggested that injections of suspensions of *M. leprae* in the form of leprolin may further increase the resistance, especially if injected around lesions showing cellular response, and also perineurally. Injections of 1 in 10 and 1 in 20 Hansen's leprolin intradermally into the macules and around their margins appear to be promising, intervals of one or two months being sufficient in some cases. They should not, however, be used in advanced cases with low resistance except in those negative to Hansen leprolin, but positive to Stefansky's leprolin, when the latter may be used. The leprolin test is also of great value as a guide to discharging advanced nodular cases, who should be kept under observation until a moderately strong reaction is obtained to Hansen's leprolin.

L. R.

ITAKURA (Teiju). Zahnärztliche Untersuchungen bei Leprakranken.

I. Bericht: Befunde ueber Zahnausfall, Weisheitszahnausbruch und Zahnkaries besonders bei leprakranken Formosa-Chinesen (Fokien-Stamm). [**Dental Studies in Leprosy.**]—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1935. Feb. Vol. 34. No. 2 (359). [In Japanese pp. 195-211. [31 refs.] German summary pp. 211-213.]

Data are recorded from a study of the dental changes in 162 Formosan lepers, who did not show very striking differences from those of normal persons. The longer the duration of the disease the worse the dental conditions. The average loss of teeth in the lepers was 3.64, or apart from the wisdom teeth 1.81, and there was no difference between nerve and nodular cases. The average number of carious teeth in lepers was 2.40, and there were more in women than in men and in nerve than in nodular cases. In summing up the author says that he found no great difference between the teeth of lepers and healthy persons, but it is interesting to note that there was proportionately more severe disease of the front teeth of the upper maxilla than of the other teeth of lepers.

L. R.

BARGEHR (Paul). Zur Leprafrage. [**The Leprosy Question.**].—*Muench. Med. Woch.* 1935. Jan. 10. Vol. 82. No. 2. pp. 56-57.

The author deals further with the results of his cutireaction in leprosy in relation to epidemiology and immunization. A sterile extract of lepromata rich in bacilli is injected intradermally and the results are given in four classes: 1. Those who have never come into contact with lepers give a negative reaction, as there has been no opportunity for the formation in the system of antibodies. 2. Those who have lived for long in contact with lepers, but have remained healthy, give a positive reaction, because as the result of infection they have developed antibodies which have destroyed the infection. 3. Persons who have developed active bacteriologically positive leprosy give a negative reaction, because they have developed antibodies insufficient to overcome the infection. 4. Persons who have lost all active symptoms of leprosy, and passed into a quiescent recovered stage, give a positive reaction, because they have developed sufficient antibodies. He also maintains that by giving 2 to 4 or more intradermal injections of his leprolin immunity can gradually be produced, and he thinks this may prove of value in combating the disease.

L. R.

MUIR (E.) & CHATTERJI (K. R.). Factors influencing the Spread of Leprous Infection.—*Indian Med. Gaz.* 1934. Sept. Vol. 69. No. 9. pp. 495-500. With 3 figs. & 6 charts.

The first part of this paper deals with the leprolin test on the lines of his previous ones. In the second part the author records with diagrams the incidence of leprosy in six affected families, and he points out that of 17 persons in house contact with lepers up to six years of age 10 had already become infectious cases; all from persons classed as infectious. The young, who are usually positive to the leprolin, are much more susceptible than non-reacting adults owing to lower resisting power.

L. R.

TISSEUIL (J.). Quelle est la durée minima d'incubation de la lèpre ? [**Minimum Incubation Period of Leprosy.**].—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 60-62.

Infection in infants has been studied to find the shortest incubation period, and in several cases this has been found to be only three months owing to the great susceptibility of young children.

L. R.

CHIYUTO (Sulpicio). Early Leprotic Changes in Children and their Bearing on the Transmission and Evolution of the Disease. II.—*Monthly Bull. Bureau of Health.* Manila. 1934. Dec. Vol. 14. No. 12. 34 pp. [18 refs.]

This paper is a continuation of a previous study of 40 cases in the Philippines [this *Bulletin*, Vol. 31, pp. 5 & 866] and confirms the data of the earlier one. The most common lesions noted are multiple depigmented areas or macules in 35 per cent. of the cases, minute papular-vesicular eruptions in 42.5 per cent., and in 41.6 per cent. of cases formerly without nerve symptoms small areas of anaesthesia have developed. Since the last report 27.5 per cent. of the lesions

have remained stationary, 20.0 per cent. have slightly advanced, 35 per cent. moderately, and 17.5 per cent. markedly so. In all only 22.5 per cent. have progressed to typically leprous manifestations.

L. R.

LARA (C. B.) & DE VERA (B.). **Clinical Observations with Reference to Leprosy in Children of Lepers.**—*Jl. Philippine Islands Med. Assoc.* 1935. Mar. Vol. 15. No. 3. pp. 115–129.

These workers have examined 240 children of leper parents and 78 control ones for skin lesions suspected by CHIYUTO to be early leprosy, and, with the exception of enlarged cutaneous nerves, contracture of the fingers and flushing of the legs, they met with them also in the children of non-leper parents, the hazy pale areas being found in 50 per cent. of the latter class. The depigmented areas, goose-flesh condition and the neurotrophic changes were also found in similar aged children of non-leper parents, the last in even greater numbers than in the children of lepers, but markedly ichthyotic condition of the legs was more common in the latter class. The total incidence of suspected lesions among the children of lepers was far less than CHIYUTO reported.

L. R.

WADE (H. W.) & LE ROUX (J. J. du Pré). **A Leprosy Case Progress Chart.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 33–42. With 3 figs. & 1 folding chart.

This chart will be of value in enabling systematic clinical records to be made of leprosy cases.

L. R.

TÔYAMA (Ikuzo) & ISHIZU (Shun). Ueber den leprösen Haarausfall. (Klinische Untersuchung.) [**Loss of Hair in Leprosy.**]—*Japanese Jl. Dermat. & Urol.* 1935. Jan. Vol. 37. No. 1. [In Japanese pp. 56–95. With 22 figs. [19 refs.] German summary pp. 9–40.]

This is an elaborate tabulated analysis of the incidence of loss of hair in leprosy patients, of whom 20.8 per cent. showed no loss of hair, and 79.2 did show such loss. The eyebrows were affected in 80 per cent., the head in 69, the beard in 43, the axilla in 50 and the pubic hairs in 47 per cent. Females suffered slightly more often than males, except as regards the head. The proportion affected increased with the age up to 50, and later fell. In nodular cases 99 per cent. were affected, in macular cases 84 and in nerve cases only 71 per cent.

L. R.

STEIN (A. A.). **The Skin Temperature in Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1934. Oct.–Dec. Vol. 2. No. 4. pp. 403–411. With 3 figs.

The author concludes from his study that the skin temperatures are usually higher in dermal leprosy owing to the vascularity of infected tissue, especially in young lesions and reacting ones. In neural leprosy the temperature may be higher over macules, but it is generally lower over other lesions, and the anaesthetic areas have a lower temperature.

L. R.

FÉRON (J.). Lèpre et neuro-fibromatose. [**Leprosy and Neurofibromatosis.**—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 912-915. With 2 figs.

This is a brief report of case of leprosy and Recklinghausen's neurofibroma being met with in the same subject. L. R.

FOX (Howard) & KNOTT (James). **Leprous Nodules of the Male Genitalia.**—*Internat. Jl. Leprosy.* Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 445-446. With 1 plate.

This is a brief illustrated account of an advanced nodular leprosy case with well-marked lesions on the penis and scrotum. L. R.

MOISER (B.). **Analysis of 722 Cases of Leprosy and their Treatment.**—*Internat. Jl. Leprosy.* Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 423-429.

This paper deals with 722 cases of leprosy treated in 1931-34 at the Ngomahuru Leper Hospital of Southern Rhodesia, all negroes except one, and including 80 children, all but one infected before admission. Conjugal infections were 6.6 per cent. Neural cases formed 45, cutaneous 2 and mixed 53 per cent. of the total. Regular occupation and exercise is provided by gardening, etc. Alepol and ethyl esters form the "specific treatment," chiefly the latter in the iodized form as it is less irritant, 10 cc. being injected once a week intramuscularly and intradermally, and with one or two weeks remission after seven weeks treatment. Trichloroacetic acid is applied to nodules and raised macules. The results show among N1 cases 55 discharged arrested and 38 likely to be so soon, or 95 per cent. of good results. Of 106 N1-C1 cases 8 are discharged, 77 improved, and a total of 46 per cent. have become bacteriologically negative and most of them will probably be discharged in time. "So it can be said that over 90 per cent. of our early cases can be arrested—and called cured if we do not quibble about the word." Only 14 were purely cutaneous and 1 is discharged and 6 others improved. Improvement in some degree has been shown in all except the advanced N3-C3 type, which are few and their treatment is of doubtful value, but occasionally an apparently hopeless case shows remarkable improvement. Microscopical examinations are made four times a year and give the best indication regarding progress, for with improvement the bacilli become less deeply stained, scattered and dotted. The work is still deficient as regards following up discharges and examining contacts of known cases, which is a much better way of getting early cases than a general survey. L. R.

- i. MONTEL (M. L. R.). Poussées de lépromes furonculoïdes au cours du traitement par le bleu de méthylène. [**Furunculosis in Methylene Blue Treatment.**—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Jan. Vol. 13. No. 1. pp. 9-12.
- ii. DOROLLE (P.) & NGO-QUANG-LY. Lèpre mixte et polynévrite à marche aiguë. Traitement par le bleu de méthylène. Guérison rapide de la polynévrite. Arrêt et régression de l'évolution lépreuse.—*Ibid.* pp. 16-20.

i. Montel records that the methylene blue treatment in leprosy predisposes to the development of pustules and acne over the lesions,

but he does not consider this a contraindication unless prolonged and extensive, as he thinks it favours the resolution of the leprous lesions. The condition is favourably influenced by lugol intravenously or by eosinosate of caesium.

ii. This is a report on an advanced mixed case of leprosy showing great improvement in all respects under methylene blue treatment.

L. R.

DUBOIS (A.), WESTERLINCK (H.) & DEGOTTE (J.). Essais thérapeutiques dans la lèpre. Le bleu de méthylène. [**Methylene Blue in Leprosy.**].—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 63-67.

The treatment of 15 leprous negroes by Montel's methylene blue solution intravenously is reported on with totals of 3 to 6 gm. of the drug. The results were completely negative, and they suggest that possibly the photodynamic action of the drug deposited in the skin lesions may be inhibited by the pigment of black races, although against this they point out that RYRIE obtained negative results with this dye in the Orient.

L. R.

LÉPINE (P.) & MARKIANOS (J.). Action directe du bleu de méthylène sur le bacille de Hansen dans l'organisme humain. [**Action of Methylene Blue on Hansen's Bacillus.**].—*C. R. Soc. Biol.* 1935. Vol. 118. No. 1. pp. 9-10.

In view of MONTEL's results from intravenous injections of methylene blue the authors have tested the action of the dye on lepra bacilli by puncturing leprous lesions after intravenous injections of the dye, and staining the bacilli and cells in the exudate by Ziehl's method. After the first injections no changes in the number of staining properties of the organisms were noted, but, even before the lesions showed obvious changes apart from the blue staining, some of the bacilli showed an irregular granular aspect, and later they stained blue, and not red, by the Ziehl method. These changes increased to indicate a direct action of the dye in producing progressive degeneration of the microbes.

L. R.

MARCHOUX (E.) & CHORINE (V.). Action du bleu de méthylène sur les lépromes "in vivo." [**Action of Methylene Blue on Lepromas.**].—*Bull. Acad. Méd.* 1935. Jan. 8. 99th Year. 3rd Ser. Vol. 113. No. 1. pp. 10-12.

The authors have investigated the action of methylene blue on lepromes by injecting intravenously rats infected seven months previously with rat leprosy, and sacrificing them for microscopical examinations after varying intervals. The stain is reduced in living cells to a colourless product, but the lepra bacilli retain the blue colour, which may serve to convey an active substance into them, although the dye itself is not lethal to the organisms.

L. R.

NICOLAS (C.). Bleu de méthylène et lèpre. [**Methylene Blue and Leprosy.**].—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 10-11.

The author reports favourable results from intravenous injections of methylene blue, although it failed in cases in which such a chaulmoogra

preparation as hydranol had not proved successful. The dye treatment is less painful and more acceptable to the patients than hydranol.

L. R.

SICÉ (A.) & MOREAU (P.). De la surveillance de la fonction rénale au cours du traitement prolongé de certains lépreux par le bleu de méthylène. [**Renal Functions under Methylene Blue Treatment.**]—*Marseille-Méd.* 1934. Nov. 25. Vol. 71. No. 33. pp. 637-642.

The authors report that they have confirmed the good results of MONTEL from the methylene blue treatment of leprosy, but they record two cases in which after prolonged injections of the drug albuminuria was produced due to irritation of the kidney parenchyma during the excretion of the drug.

L. R.

- i. FRÉVILLE (L. H.). Note relative à quelques essais d'injections intraveineuses de solution iodo-iodurée dans la lèpre. Premiers résultats. [**Intravenous Injections of Potassium Teriodide in L.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Oct. Vol. 12. No. 8. pp. 756-758.
- ii. MONTEL (M. L. R.). A propos de la communication de Fréville quelques essais d'injections intraveineuses de solution iodo-iodurée dans la lèpre.—*Ibid.* pp. 759-760.

i. After methylene blue injections suppuration of the crural glands accompanied by fever appeared, and was treated by intravenous injections of four doses of 4 to 10 cc. of I. 1 gm. KI. 2 gm. in 300 cc. distilled water, with the result that suppuration and fever subsided completely. In two other cases of febrile reactions similar good effects were obtained.

ii. Montel confirms the above, and adds that he treated another reacting case with injections of eosinate of caesium with success after three doses.

L. R.

LAGROSA (M.), ALONSO (J. M.), TIONG (J. O.) & PARAS (A.). **Treatment of Acute Leprous Neuritis with Iodized Wightiana Ethyl Esters (with Report of Cases).**—*Jl. Philippine Islands Med. Assoc.* 1935. Feb. Vol. 15. No. 2. pp. 87-94.

Fourteen cases with thickened and inflamed nerves and great pain were treated by the injection along the course of the nerves, and sometimes into them, of from 1 to 4½ cc. of iodized ethyl esters, with rapid amelioration of the pain, frequently followed by improvement in sensation and contractures of the fingers. Four other cases injected with dilester from Fiji did not do so well.

L. R.

MONSERRAT (Carlos). **Does Chaulmoogra Treatment influence the Shifting of Serologic Findings in Lepers as obtained by the Wassermann, Kahn, and Vernes Reactions?**—*Philippine Jl. Sci.* 1934. July. Vol. 54. No. 3. pp. 343-363. With 6 figs.

The Wassermann, Kahn and Vernes reactions have been investigated before and after treatment in 84 lepers in all, 46 of whom had received no chaulmoogra injections. There was a general agreement of the three tests both before and after treatment, but the Wassermann reactions were weaker than the others. Reactions were more frequent

in those over 30 years of age, in those positive bacteriologically and in the mixed type. Prolonged chaulmoogra treatment may cause a marked decrease in the reactions, without necessarily improvement for a time, and neosalvarsan has a similar effect and is beneficial. Chaulmoogra oil may also reduce the reactions in monkeys infected with syphilis or yaws, and in both cases the Vernes reactions were changed more promptly than the others. 17.8 per cent. of the lepers gave plus reactions with all three tests.

L. R.

STÉVENEL (L.). L'épuration des huiles de chaulmoogra n'est-elle pas une erreur thérapeutique? Réflexions au sujet des injections intraveineuses d'huile. [Possible Disadvantage of refining Chaulmoogra Oil.]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 14-18.

The author suggests that the original chaulmoogra oils may be more active than preparations made from them on account of the former containing impurities such as sterol, which he thinks is more active than the oil, so the latter should be injected intravenously in a fine emulsion. [The reviewer sent to India for trial fine hydnocarpus emulsions, which were considered to be promising.]

L. R.

EMERSON (George A.) & ANDERSON (Hamilton H.). **Acute Toxicity of Ethyl Chaulmoograte.**—*Proc. Soc. Experim. Biol. & Med.* 1934. Nov. Vol. 32. No. 2. pp. 289-291.

A study has been made in rats of the toxicity of single doses of a number of ethyl ester chaulmoograte preparations with the following results:—

"Examination of the tabulated data indicate that: (1) purified ethyl chaulmoograte preparations are more toxic than the ethyl esters of the total fatty acids of chaulmoogra oil, presumably because of higher content of ethyl chaulmoograte; (2) iodizing ethyl chaulmoograte with 0.5 per cent. iodine has little effect on toxicity; (3) addition of 4 per cent. creosote increases the toxicity, commensurate with the amount of creosote present; (4) the degree of unsaturation of crude ethyl chaulmoograte is not a sufficiently sensitive index of toxicity to be reliable; and (5) if subcutaneously administered ethyl chaulmoograte exerts its toxic effect through liberation of Na chaulmoograte into the circulation, the summation of rates of hydrolysis and diffusion cannot much exceed that causing a disappearance of 2 millimols per Mol of the injected ester per hour, since Na chaulmoograte kills rats in intravenous acute doses of 0.1-0.125 gm./kg."

L. R.

COLE (H. I.). **Note on the Decomposition Products in Chaulmoogra Oils.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.-Mar. Vol. 3. No. 1. pp. 81-82.

In this brief note the author points out that in the course of his earlier work at Cullion he often noted a syrupy oil as a by product in the analysis of chaulmoogra oils, a decomposition product formed more rapidly in the presence of light and air and under tropical conditions. Pure hydnocarpic acid was transformed much more rapidly than pure chaulmoogric acid.

L. R.

EMERSON (George A.), ANDERSON (Hamilton H.) & LEAKE (Chauncey D.). **A Pharmacological Comparison of Na-Hydnocarpate ("Alepol") and Na-Dichaulmoogryl- β -Glycerophosphate ("Chaulphosphate").**—Reprinted from *Arch. Internat. Pharmacodyn. et Thérapie*. 1934. Vol. 48. No. 2. pp. 247–254. [18 refs.]

The authors state that a water soluble chaulmoograte in the form of sodium gynocardate was first used for the general systemic treatment of leprosy by L. ROGERS, with desirable results by the intravenous method, but with the drawback of blocking the veins, which is only partly overcome by MUIR's technique; alepol is the best of such preparations. With a view to further improvement the synthesis of soluble chaulmoogrates without the undesirable effects of soaps has been undertaken by Richard WRENSHALL in Hawaii, and they have been tested on rat leprosy in comparison with alepol. The best of these is sodium dichaulmoogryl- β -glycerophosphate, called for convenience "Chaulphosphate," as it has a low and reasonably constant toxicity in animals, especially intravenously; this is important because a definite correlation between available chaulmoogric acid and the beneficial effect in rat leprosy has been noted. Slow hydrolysis may have the same result as constant small injections of sodium chaulmoograte. The new preparation has a lower iodine number, is four to ten times less toxic than alepol, is not haemolytic, and highly unsaturated, and probably more active. Chaulmoogric acid is liberated from it. The use of this drug in rat leprosy compared favourably with alepol, and it has already been given to six volunteers intravenously in total amounts of 175 mgm./kgm. in two weeks in a 3½ per cent. solution. L. R.

DE SOUZA-ARAUJO (H. C.). **The Brazilian Chaulmoogra: *Carpotroche brasiliensis*. A Review.**—*Internat. Jl. Leprosy*. Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 49–66. With 15 figs. on 6 plates. [37 refs.]

A botanical description of *Carpotroche brasiliensis* is first given, and the geographical distribution and mode of culture described. Recorded chemical analyses of the Sapucainha oil derived from the seed are discussed, and its commercial products enumerated. Special fatty acids have been described by MACHADO under the terms carpotrochic and carpotrochinic acids, but DA SILVA found only chaulmoogric and hydnocarpic acids as in other chaulmoogra oils. L. R.

MONTEL (M.) & TRUONG-VAN-QUE. **Essais de traitement de la lèpre par les injections intraveineuses de résorcine. [Treatment of Leprosy by Intravenous Injections of Resorcin.]**—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 167–169.

Intravenous injections of resorcin, 40 cgm. up to 1.15 gm., in lepers had no toxic effect and appeared to improve the general health of the patients, except in one cachectic case in which albuminuria ensued. In four nodular cases no benefit resulted, and in three early cases only slight temporary reduction in the infiltration of the lesions was noted, so a more active treatment had to be adopted. I. R.

TISSEUIL (J.). Traitement de la lèpre par injections intraveineuses d'eau distillée. [**Treatment of Leprosy by Intravenous Injections of Distilled Water.**]*—Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 169–171.

The author reports two cases in which intravenous injections of distilled water apparently had a beneficial effect, especially as regards a feeling of well being and on sensory symptoms. L. R.

LOEWENSTEIN (E.). **The Cultivation of the Leprosy Bacillus. Preliminary Communication.***—Internat. Jl. Leprosy.* Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 43–47.

Many years' work on the cultivation of the leprosy bacillus has convinced the author that the presence of saprophytic diphtheroids and other organisms in symbiosis with that of leprosy make such tissues unfavourable for obtaining pure cultures of the latter, so he has attempted to do so from the blood of lepers. It should be citrated and dehaemoglobinized by the addition of sterile distilled water and centrifuged three times. The deposit is then treated with 1 cc. of 15 per cent. sulphuric acid for five minutes and again washed twice, and glycerine egg and other media to which fish broth has been added inoculated. In two out of five cases a pure culture of acid-fast bacilli, and in two both tubercle and leprosy bacilli were obtained. The growth is so slow that it takes up to six months to get visible colonies. They produced acid and were not infective to guinea-pigs. L. R.

LOWE (John). **A Note on the Application of Tissue Culture Methods to Leprosy Research.***—Leprosy in India.* 1935. Jan. Vol. 7. No. 1. pp. 19–22.

This is a brief review of former work on attempts to grow the lepra bacillus in tissue cultures by SALLE, TIMOFEJEWSKY and by MCKINLEY and VERDER. Lowe reports that he has failed to confirm the work of the last two, but thinks further trials are required. L. R.

DUVAL (Charles W.). **Morphological and Tinctorial Behavior of *B. leprae* during its Adaptation to an *in Vitro* Habitat.***—Proc. Soc. Experim. Biol. & Med.* 1934. Dec. Vol. 32. No. 3. pp. 498–503.

In view of very varying morphology attributed to the *M. leprae* in cultures the author has studied its changes in *in vitro* tissue cultures of leprosy material by staining portions in different ways at various intervals of time in the course of six months' culture. The globi first disappear and the bacilli become more rounded at the ends. The granules or beads may be seen at either pole producing a diphtheroid appearance, while others have 4 to 6 granules. Free granules may be seen at times, but not after the bacilli gain the power of saprophytic growth. The acid-fast characters are retained throughout and they are positive to Gram's stain. Loeffler's methylene blue shows the intra- and extracellular granules to be metachromatic.

L. R.

POOMAN (A.). Die McClure-Aldrich-Quaddelprobe bei Leprösen. [The McClure-Aldrich Wheal Test in Leprosy.]—*Arch. f. Schiffsh. u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 121–123. [10 refs.]

The author reports on trials of the McClure-Aldrich intradermal wheal test (Q.R.Z.) in 14 cases of leprosy, one of whom was a recovered patient. Two cc. of physiological salt solution is injected intradermally, and also Q.R.Z. antigen. In healthy persons absorption takes 60 to 90 minutes, or in the author's controls an average of 58 minutes. In 7 nodular lepers the time was from 17 to 39 minutes, in 4 maculo-anaesthetic cases 25 to 48 minutes, in 1 mixed case 27 minutes and in 1 tuberculoid case 17 minutes.

L. R.

HOFFMANN (W. H.) & BAEZ (Pedro Ramos). **Allergic Erythematous Eruptions in Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1935. Jan.–Mar. Vol. 3. No. 1. pp. 23–32. With 2 figs. on 1 plate.

This is a brief report of two cases showing Herxheimer's reaction. It is followed by a theoretical discussion in which the authors assume the occurrence of a pre-bacillary period, which may produce sufficient toxin to create a state of sensitivity, and this may later give rise to an allergic reaction when a large number of bacilli are destroyed and their toxins liberated, to produce a congestive and anaphylactic eruption.

L. R.

PARMAKSON (Paul). Ueber die eosinophilen Zellen im Blutbilde der Leprakranken. [The Eosinophiles in Leprosy.]—*Dermat. Woch.* 1935. Mar. 9. Vol. 100. No. 10. pp. 285–288. [13 refs.]

From the examination of the blood of 24 lepers the author concludes that eosinophilia is not characteristic of leprosy, for in active untreated cases he found a fall in the number of eosinophiles, and normal counts or a slight increase in latent cases. The fluctuation in their numbers is determined by variations in other infections of the patients. Successful treatment is followed by some increase.

L. R.

OTA (Masao) & ISHIBASHI (Takeo). **Complement-Fixation Reaction of Lepers' Sera with Bacillary Antigens.**—*Internat. Jl. Leprosy.* Manila. 1934. Oct.–Dec. Vol. 2. No. 4. pp. 413–422.

The authors' complement-fixation tests agree with those of others in showing that different strains of acid-fast bacilli cannot be distinguished by their means. On the other hand, they found that Ota and Sato's Bg strain in particular gave a very high percentage of positives with leper's sera, and almost negligible ones with non-leprous sera. Illustrative tables are given and the technique is described. They think that with the isolation of the chemical elements of the bacteria it may become possible to differentiate the bacilli also, and they believe the ether-soluble elements are most concerned in such specificity.

L. R.

BULKIN (A.). The Complement Fixation with Leprous Antigens in Leprosy.—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1-2. [In Russian pp. 36-38. English summary p. 38.]

The author describes the results of the complement fixation test with 101 samples of serum (84 from cases of leprosy and 17 from non-leprous ones, including 3 cases of syphilis and 1 of tuberculosis). Bacterial, testicular and complex (bacterial + testicular) antigens were employed. The highest percentage of positive results was obtained with the bacterial antigen, the lowest with testicular, while the tests with all the non-leprous sera were negative. *C. A. Hoare.*

MILASCH (G. P.). Ueber die Veränderung des elastischen Gewebes bei Lepra. [**Changes in Elastic Tissue in Leprosy.**]—*Virchows Arch. f. Path. Anat. u. Physiol.* 1934. Vol. 292. No. 2. pp. 216-219. With 1 fig.

This is a brief paper describing and illustrating the disintegration of the elastic fibres in the skin of a proliferating leproma. *L. R.*

BLACK (Sam H.) & ROSS (Hilary). Blood Cholesterol in Leprosy. A Study of the Total and Free Cholesterol, Cholesterol Esters, Van den Bergh Reaction, and the Complement Fixation Test.—*Public Health Rep.* 1935. Jan. 11. Vol. 50. No. 2. pp. 50-59. [15 refs.]

The blood of 200 lepers and of 20 healthy young adults was examined for total and free cholesterol, cholesterol esters and the percentage of esters, and the sera used for the van den Bergh reaction and the complement fixation test. The esters were higher in lepers and highest in those retrograding. Serum bilirubin was positive in 138 cases. There was no correlation between complement fixation and the cholesterol. *L. R.*

RODRIGUES DE ALBUQUERQUE (A. F.). Sur l'isolement d'un bacille acido-résistant d'un lépreux. [**Isolation of Acido-Resistant Bacillus from a Leprome.**]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 7. pp. 713-715.

Cultures were made from two leprosy nodules removed from a patient, titrated in a sterile manner with salt solution and inseminated on glycerine jelly and broth, Petroff's and Petragnani's media. On the last after eight days whitish yellow colonies of an acid-fast bacillus were obtained which retained their characters to the third subculture. *L. R.*

GILLIER (M. R.). Une méthode sérique simple différenciant la lèpre et la syphilis (note préliminaire). [**Differentiation of Leprosy and Syphilis Serologically.**]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 915-917.

By the formol-gel and the reaction of Meinicke leprosy and syphilis give similar reactions except that tolu-antigen gives a positive result with syphilitic and a negative one with leprosy sera. *L. R.*

- i. BERNY (P.). La bacillurie chez les rats lépreux. [**Rat Leprosy.**]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 910–912.
- ii. PRUDHOMME (R.). Action des rayons X sur les lépromes des rats.—*Ibid.* pp. 917–920.
- iii. BERNY (P.). Conservation de la vitalité du bacille de Stéfansky chez le cobaye.—*Ibid.* 1935. Jan. 9. Vol. 28. No. 1. pp. 5–7.
- iv. PRUDHOMME (R.). Influence du pH sur la conservation du bacille de Stefanski en bouillon glyciné.—*Ibid.* pp. 11–14.
- v. THIROUX (A.). Essais de chimiothérapie de la lèpre du rat.—*Ibid.* pp. 18–21.

i. The first of this series of short papers on rat leprosy records observations of Berny to show that bacilluria does not normally occur in the disease, but it may be induced by administering novarsenobenzol, but not by potassium iodide.

ii. Prudhomme reports that radiation at the site of inoculation of rat leprosy bacilli does not prevent infection, although it retards its evolution. Cells parasitized by the organism are more rapidly destroyed by X-rays than normal cells, but bacilli set free by destroying the cells retain their vitality for at least ten days.

iii. Berny has investigated the period of survival of Stefansky's bacillus when injected into guineapigs, which are immune to infection, and found that they remained infective for rats up to 39 days, but died between 39 and 45 days.

iv. Prudhomme has tested the influence of pH on the survival of Stefansky's bacillus in glycerine broth, and concludes that it only flourishes in a pH between 6 and 7, with an optimum of 6.4.

v. Thiroux reports on the treatment of leprosy rats, with controls, by injections of some new chemotherapeutic preparations of nickel, cobalt and arsenic supplied by Professor FOURNEAU and M. TRÉFOUEL. Only temporary retardation of the development of the leprosy lesions was noted, especially after the use of nickel, and the subsequent evolution of the disease was as complete as in the controls. L. R.

BERNY (P.). Un séjour de 24 h. *in vitro* dans le bleu de méthylène à 0.5 p.o/o n'atténue pas la virulence du bacille de Stéfansky. [**Attempted Attenuation of Stefansky's Bacillus by Methylene Blue.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 58–59.

The action of methylene blue *in vitro* on the rat leprosy bacillus has been tested by making a bacillary emulsion from an intraperitoneal leprosy removed from an infected rat, and mixing with an equal volume of a 1 per cent. solution of the dye. After keeping at blood heat for 12 to 24 hours the emulsion was injected into six rats, only two of which survived the dose, and he found months later both had developed rat leprosy; so the strong solution of the dye had no effect in attenuating the organism. L. R.

LAMB (Alvin R.). **The Effect of Malnutrition on the Pathogenesis of Rat Leprosy.**—*Amer. J. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 438–455. With 6 figs.

The author points out that there is some general relationship between diet deficiencies, especially such as produce beriberi, and the

distribution of leprosy; this has led him to study the question experimentally in rats inoculated with material from rat lepromata, either subcutaneously or intra-cardially, on normal and on deficient diets. The subcutaneous inoculations of rats on diets of varying deficiencies generally yielded negative results, but after intracardiac inoculation rats on diets deficient in vitamin B complex, and with somewhat low protein, showed extensive increase in the lepromatous lesions in the liver more particularly as compared with the controls, and to a less extent with regard to the spleen, lungs and lymph nodes. Similar changes were found in fourth generation rats on a diet less deficient in vitamin B.

L. R.

CHOUCROUN (Nine) & PELTIER (Maurice). Sur l'ultravirus de la lèpre murine. [**The Ultravirus of Rat Leprosy.**].—*C. R. Acad. Sci.* 1935. Feb. 25. Vol. 200. No. 9. pp. 785-787

The question of the occurrence of an ultravirus filterable stage of the organism has been reinvestigated to determine if any visible bacilli are present in the filtered material which gave rise to rat leprosy on inoculation into those animals. Chamberland bougies L2 and L3 were used, and the filtrates were subject to a 40 volt-cm current for an hour and a half, and then the fluid on the anode poles, which attract any particles, was examined minutely, with the result that in four of six experiments a small number of bacilli were demonstrated. This indicates that a few of Stefansky's bacilli had passed through the filters and explained infection of rats by such filtrates, and not by the ultravirus of Markianos.

L. R.

AFANADOR (A.). Evolution de la formule leucocytaire chez le rat lépreux. [**The Leucocyte Formula in the Leprous Rat.**].—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 67-70.

Healthy rats show a high proportion of lymphocytes, but in rat leprosy with the development of the disease they tend to be replaced by polynuclears and large mononuclears, especially when suppuration takes place.

L. R.

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- BOURGUIGNON (G. C.). Nouveau cas de lèpre diagnostique au Congo Belge chez un Européen.—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 389-392. With 2 figs.
- BURKITT (R. W.). Case of Leprosy treated by Intravenous Injections of Methylene Blue.—*East African Med. Jl.* 1935. Feb. Vol. 11. No. 11. pp. 356-358.
- CHATTERJI (S. N.). The Age of Danger for Leprosy.—*Internat. Jl. Leprosy.* Manila. 1935. Jan.-Mar. Vol. 3. No. 1. pp. 82-83.
- DOROLLE & NGO-QUANG-LY. Essai d'emploi dans le traitement de la lèpre d'un colorant composé: bleu de méthylène-éosine.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Jan. Vol. 13. No. 1. pp. 21-24.
- DUTTA (Nirmal Chandra). An Encouraging Result obtained by the Use of E.C.C.O. in the Early Stage of Leprosy—Anaesthetic Type.—*Indian Med. Gaz.* 1934. Dec. Vol. 69. No. 12. pp. 688-689.
- FENG (C. T.) & CHENG (C. L.). A Preliminary Report on the Use of Benzyl-ephedrine-Chaulmoogra Oil in the Treatment of Leprosy.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 741-747. With 14 figs. on 5 plates & 1 text fig.

- HOFFMANN (W. H.) & RAMOS BAEZ (Pedro). Los brotes fluxionarios de la alergia en la lepra.—Reprinted from *Jl. d. Clinicos*. 1934. July 15. No. 13. 28 pp. With 2 figs.
- HUIZENGA (Lee S.). Anhydrosis and Alopecia in Leprosy. A Report on Two Hundred Cases.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 715-720.
- LOWE (John). A Note on the Staining of *Mycobacterium leprae* in Tissue Sections.—*Indian Jl. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 313-315.
- MONTÉL (M. L. R.). Traitement de la lèpre par le bleu de méthylène en injections intraveineuses.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 753-775. [13 refs.]
- MONTÉL (M. L. R.) & NGUYEN-NGOC-NHUAN. Un cas de lèpre trophoneurotique et maculeuse traité par les injections intraveineuses de bleu de méthylène. Bilan après 8 mois de traitement.—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Nov. Vol. 12. No. 9. pp. 812-823.
- MONTÉL (R.) & TRUONG-VAN-QUE. Le "rouge neutre" en injections intraveineuses dans le traitement de la lèpre. (Note préliminaire).—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 715-716.
- OTA (M.), SATO (S.) & ISHIBASHI (T.). Contributions à la sérologie et à la thérapie de la lèpre.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 729-740.
- PUESTE (José J.) & FIOL (Héctor). Extirpación quirúrgica de las lesiones iniciales de la lepra.—*Semana Méd.* 1935. Jan. 10. Vol. 42. No. 2 (2139). pp. 117-120.
- REISS (F.). The Therapeutic Value of Sodium Thiosulphate in the Treatment of Leprosy.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 777-781.
- RIBEIRO (Leonidio). A lepra é capaz de alterar as impressões digitais.—*Folha Méd.* 1934. Sept. 25. Vol. 15. No. 27. pp. 315-316.
- RIBEIRO (Leonidio). La lèpre est capable d'altérer les dessins papillaires des empreintes digitales.—*Bull. Acad. Méd.* 1934. Dec. 18. 98th Year. 3rd Ser. Vol. 112. No. 41. pp. 821-822.
- RYRIE (G. A.). The Present Position of Dye Therapy in Leprosy.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 749-752.
- SCHOUTE (D.). Enkele volksplagen in het verleden van Nederlandsch Indië. [Leprosy].—*Nederl. Tijdschr. v. Geneesk.* 1935. Apr. 6. Vol. 79. No. 14. pp. 1587-1604. [13 refs.]
- DE SENA (Michelangelo). Il funzionamento del Lazzaretto di Mogadiscio nel biennio 1932-1934.—*Arch. Ital. Sci. Med. Colon.* 1935. Feb. 1. Vol. 16. No. 2. pp. 135-147. With 4 figs. [16 refs.] English summary (3 lines).
- SOULE (M. H.). Cultivation of *Mycobacterium leprae*. III.—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1197-1199.
- SOULE (M. H.). Bacteriology of Leprosy. IV. Bacteremia.—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1200-1201.
- WADE (H. W.). A Case of Neuritis of the Lateral Femoral Nerve.—*Internat. Jl. Leprosy*. Manila. 1934. Oct.-Dec. Vol. 2. No. 4. pp. 451-454.
- WADE (H. W.). Tuberculoid Leprosy and its Classification.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 1. pp. 685-697. [34 refs.]
- WALKER (Ernest Linwood) & SWEENEY (Marion A.). Cultivation of Facultative Acid-Fast Bacteria from Filtrates of Leprosy.—*Proc. Soc. Experim. Biol. & Med.* 1934. June. Vol. 31. No. 9. pp. 1162-1163.
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THE TYPHUS GROUP OF FEVERS.

RIDING (D.). *The Typhus Group of Fevers.*—*Jl. Egyptian Med. Assoc.* 1935. Mar. Vol. 18. No. 3. pp. 147–161. [10 refs.]

The first part of this paper consists of a brief summary of present day knowledge of the typhus group of fevers. An up-to-date and comprehensive table is given.

In the early months of 1933 a large number of cases of typhus occurred in Egypt. Blood was taken from a typical case on the 6th day of fever and injected into two guineapigs; both developed fever after an incubation period of 13 days. The virus was passaged to other guineapigs. In no case was the Neill-Mooser reaction noted in any of the infected guineapigs. Rabbits inoculated intraperitoneally with brain emulsion of infected guineapigs developed agglutinins for OX19 to a titre of 1/250. Inapparent infections were produced in rats. The virus was the "classical old world epidemic typhus."

One hundred and thirty wild rats and mice were captured in Cairo and examined but no strain of typhus virus could be isolated from them.

An interesting *Haemophilus bacillus* resembling *Rickettsia* was isolated from some of the wild rats and is described. *D. Harvey.*

JOURNAL OF THE ROYAL ARMY MEDICAL CORPS. 1935. Mar. Vol. 64. No. 3. p. 187.—*The Typhus Group of Fevers.*

The classification as displayed in attached table and based on the serological reactions of the typhus fevers is suggested by FELIX as preferable to classification according to the vectors. [In this table São Paulo typhus is shown as "undetermined" but the sera of cases of this disease have been shown to agglutinate X19 in high dilution and XL (Lima) in a similar manner.]

Typhus Group of Fevers.

Subgroup	Type X19	Type XK	Type undetermined
Name of disease	<i>Classical epidemic typhus</i> Tabardillo endemic typhus (Brill's) of U.S.A. and Australia, Greece, Syria, Manchuria, Malaya (shop typhus) and Toulon (fièvre nautique)	<i>Japanese river fever</i> (Tsutsugamushi fever of Japan, Malaya and Dutch East Indies) Malay scrub typhus, Scrub typhus of East Indies	<i>Spotted fever of Rocky Mountains</i> São Paulo endemic typhus, Fièvre boutonneuse, Febbre errutiva, Tick bite fever of S. Africa, India tick typhus
Vector	Lice and rat fleas	Mites	Ticks
Reservoir of virus	Rats Man	Field mice and rats	Rodents Dogs ? Ticks
Agglutination	X19+++ X2 + XK -	X19- X2 - XK +++	X19+ X2 + XK +

D. H.

JAME (L.) & AUJALEU (E.). Les fièvres typho-exanthématiques ou rickettsioses. [**The Typhus Fevers or Rickettsias.**]—*Arch. Méd. et Pharm. Milit.* 1935. Mar. Vol. 102. No. 3. pp. 445–498. [154 refs.]

This able paper consists of a full review of the subject of the typhus fevers. Historic typhus, Brill's disease (endemic typhus), boutonneuse fever, Rocky Mountain fever, Japanese River fever and tropical typhus are all reviewed from the clinical and epidemiological aspects and the different types are contrasted and compared.

The one main common feature in all is the presence of Rickettsia. The Weil-Felix reaction is also referred to and a bibliography of over 150 periodicals is appended. *D. H.*

RONSE (Marguerite). Contribution à l'étude du typhus exanthématique. [**Contribution to the Study of Typhus.**]—*Ann. Inst. Pasteur.* 1935. Mar. Vol. 54. No. 3. pp. 341–382. With 7 figs. [47 refs.]

The conclusions of this comprehensive paper are to this effect :—

1. The virus of endemic typhus can infect other rodents besides rats, notably the grey mouse, dwarf mouse, field mouse and the dormouse ; of these the field mouse and the dwarf mouse were most susceptible.

2. Besides rodents, hedgehogs and pigeons were also infected with the virus.

3. In addition to infection by the bite of ectoparasites, rodents can be infected by the digestive route either by feeding on infected parasites or by devouring the carcasses of animals which have died of the disease ; as a rule the disease acquired in this manner is less severe than that following injection of the virus or the bite of ectoparasites.

4. The Weil-Felix reaction was found to be positive in rats, mice and pigeons.

5. The author found that it was not possible to cultivate the virus in conjunction with moulds or fungi as SILBER had suggested.

6. Acting on the resemblance between Rickettsia and Bartonella a drug Solganal B, which has been found useful in the treatment of Carrion's disease, was given a trial on animals infected with typhus but with little or no effect on the course of the fever. *D. H.*

NICOLLE (Charles) & GIROUD (Paul). Non-transmission au rat, par ingestion, du virus typhique historique contenu dans des poux infectés. [**Rat not infected by Ingestion of Lice containing Historic Typhus Virus.**]—*C. R. Acad. Sci.* 1934. Nov. 26. Vol. 199. No. 22. pp. 1169–1170.

Some research workers have suggested that the rat virus of typhus when carried to man by the rat flea may become a human virus and be passed from man to man by the louse ; if this be so Nicolle enquires "How is the human virus re-transferred to the rat." One method might be by the rat swallowing infected lice and becoming infected through intestinal absorption, in the same way that rats become readily infected by eating rat fleas infected with the murine virus.

The authors carried out a series of experiments by feeding lice on typhus patients and subsequently feeding these infected lice to rats ;

none of the rats became infected ; another proof of the difference between the murine and human virus. D. H.

NICOLLE (Charles) & GIROUD (Paul). Etude des rapports du typhus exanthématique historique et du typhus murin en Tunisie. Résultats d'une enquête sur l'existence du virus murin chez les rats de foyers de typhus historique invétérés et étients ou en activité. [**Relations of Historic and Murine Typhus in Tunis.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 8-28.

The authors have shown that the virus of endemic typhus can be readily isolated from the rats in Tunis ; 4 per cent. of rats examined gave a positive Weil-Felix reaction. In spite of the presence of the murine virus especially in the dock rats there have been no outbreaks of louse-borne typhus in the city for the last 23 years ; this is due in the opinion of the authors to the careful lousing of people (nomads) entering the city from the interior. A few cases of endemic typhus have been noted but no spread of the disease although there are people in the city who are infested with lice. It is argued that these facts are further proof that the murine virus does not give rise to epidemics of louse borne typhus.

Further investigations were undertaken in places in the country where typhus had been epidemic but had not been reported for a good many years. Such places were the two convict prisons of Porto-Farina and Djouggar. The rats met with there were *Mus alexandrinus* whereas in Tunis the common rat is *M. decumanus*. One hundred rats were examined in the old fort but none gave a positive Weil-Felix reaction and no typhus virus could be isolated ; the same result was obtained at Djouggar. Investigations were then carried out among populations where louse borne typhus fever occurs every year, that is among the nomadic tribes in the desert country and mountain regions. Some 200 rats and mice caught in these areas were examined but in none was any evidence obtained of the presence of a true typhus virus. We have therefore the following contrast :—In Tunis, rats infected with typhus virus but no cases of true typhus. In the country, numerous cases of true typhus among the nomadic people but no evidence of typhus infection among the rat population. D. H.

NICOLLE (Charles) & GIROUD (Paul). Recherche des cas inapparents dans les foyers typhiques épars et mobiles du bled tunisien en 1934. [**Search for Cases of Inapparent Typhus among the Nomads in the Country round Tunis.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 29-46.

Three methods were employed in this research : (1) The Weil-Felix reaction ; (2) Inoculation of the blood of people who gave a positive reaction into guineapigs (10 cases) ; (3) feeding of lice on the same people and search for the virus in these lice.

The results of the Weil-Felix reaction are given in detail for each village or camp. Of 170 people examined 38 gave a positive reaction. 30 up to a dilution of 1/50, 6 to 1/100 and 2 to 1/200. None of these people had had any fever recently and therefore eight of them may be said to be inapparent cases of typhus. The blood of 10 people was injected into guineapigs but none reacted ; lice fed on three of these gave

also negative results, no Rickettsia were seen and injection of emulsion of the lice into guineapigs was negative. *D. H.*

NICOLLE (Charles) & GIROUD (Paul). Faits expérimentaux contraires à l'hypothèse de la transformation naturelle actuelle du virus typhique murin en virus historique, donc à l'unité actuelle de ces virus. [**Experimental Observations opposed to the Hypothesis of Transformation in Nature of Murine into Historic Virus.**]*—Arch. Inst. Pasteur de Tunis.* 1935. Jan. Vol. 24. No. 1. pp. 47–55.

The authors agree that the two typhus viruses, human and rat, have a common origin and that the rat virus is the older of the two. But they do not consider that at the present time it is possible to change the one virus into the other in the laboratory or that this process goes on, as some people think, from time to time naturally. Other workers have announced that they have succeeded in changing the rat virus into the human and *vice versa*, but Nicolle points out that this so-called change has been carried out in the guineapig, an animal which has no place at all in the story of typhus in nature, however useful it may be as an experimental indicator of infection in the laboratory. The guineapig is “un intrus” in the typhus story, an interloper.

It is true that a rat virus may lose its power of producing scrotal reaction in the guineapig and that a human virus may acquire it, but that only concerns the guineapig and does not change the human virus into the rat virus or *vice versa*.

If the rat virus can be changed into the human virus then it should be readily taken up by lice and the human virus by fleas. Experiments were carried out with this in view.

Lice were fed on monkeys which were infected with the rat virus of Tunis but none became infected. Fleas were then fed on guineapigs which were infected with the virus of human typhus but none became infected. Also rats were fed on lice which had been fed on typhus patients and contained Rickettsia but again none of the rats showed any sign of infection inapparent or otherwise.

These negative results, as the authors say, are certainly not in favour of the argument that the human virus can be changed readily into the rat virus or the rat virus into the human, and suggest that the two viruses are not identical. *D. H.*

CIUCA (M.), BALTEANU (J.) & CONSTANTINESCU (N.). Contrôle expérimental de la forme inapparente du typhus exanthématique chez l'homme. [**Experimental Control of the Inapparent Form of Typhus.**]*—C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 514–516.

An outbreak of typhus occurred in a hostel in which 20 young people were in close association; 6 cases were reported; the other 14 inmates showed no sign nor symptom of illness but the sera of all gave a positive Weil-Felix reaction at 1/100 to 1/300 dilution. 3 cc. of blood was taken from each person and inoculated intraperitoneally into guineapigs; in two instances a typical typhus reaction was obtained.

An emulsion was made from the brain of one of these infected animals and injected into a chronic nerve patient; no reaction

followed but guineapigs were infected from the blood of this man and the strain of virus was passaged to other guineapigs and to rats. These animals after the fever were shown to be immune to a second injection of the virus.

D. H.

NICOLLE (Charles) & SPARROW (Hélène). Sur la signification des réactions scrotales observées chez les cobayes inoculés avec les virus typhiques. [**On the Significance of the Scrotal Reactions observed in Guineapigs inoculated with the Typhus Viruses.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 65–69.

The authors again point out that the typhus viruses are not the only agents which may cause orchitis in guineapigs. The glanders bacillus is of course well known in this respect but should rarely be confused with typhus. On the other hand infections with bacilli allied to paratyphoid B are common in guineapigs and also in wild rats and give rise to a condition which resembles closely the scrotal reaction produced by typhus virus. The authors insist that in typhus research no scrotal reaction should be accepted as positive until cultural experiments have shown that there is no bacillary infection; the neglect of this precaution in the past has given rise to errors. Another agent which produces a scrotal reaction in guineapigs that has already been mistaken for the typhus reaction is the spirochaete of sodoku or rat-bite fever; wild rats in some districts are heavily infected with this parasite and it is readily inoculated into guineapigs. The reaction, however, is more severe and prolonged than that of typhus and smears should reveal the presence of the parasite.

D. H.

NICOLLE (Charles). A propos de six cas de typhus murin contractés au cours de recherches. [**Six Cases of Murine Typhus contracted in the Course of Research.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 99–113. With 8 charts.

The paper opens with some general remarks on the risks run by investigators generally in research laboratories, risks which are not fully appreciated by the public who benefit by these researches.

It is noted that since 1909, in spite of the fact that a great deal of work has been done in the author's laboratory at Tunis on louse-borne typhus, only one case of laboratory infection has occurred; but in the short period since 1931 in which flea borne typhus has been investigated six cases have occurred. It is comparatively easy to avoid infection by lice in a well run laboratory but at certain seasons of the year in Tunis there is such a rapid multiplication of fleas on the experimental animals and on captured wild rats in the laboratory that it is difficult to avoid infection spreading among the animals and to the personnel. Two measures of prevention are suggested. (1) destruction of ectoparasites of the animals; (2) protection of personnel by means of a special vaccine. Full notes and temperature charts are given of the six cases.

D. H.

MEDULLA (Candido). Le malattie del gruppo tifo esantematico che si osservano in Cirenaica. [**The Typhus Group of Fevers seen in Cyrenaica.**—*Arch. Ital. Sci. Med. Colon.* 1935. Jan. 1. Vol. 16. No. 1. pp. 7–39. With 22 figs. (1 map). English summary (2 lines.)]

The author analyses 49 cases of typhus fever observed during 14 years, 1921–34. He divides them on clinical grounds into four types, according to the duration of the fever, the character and extent of the rash, the involvement of the nerve centres, and the Weil-Felix reaction.

Type 1 corresponds, says the author, with the common Mediterranean form, type 2 with boutonneuse fever, type 3 with mild endemic exanthematic typhus, and type 4 with the classic exanthematic typhus. Twenty-six of the cases were of the first type, a comparatively mild form, with fever for 10–11 days, no cerebral involvement, and absent Weil-Felix reaction; there were five of the second type and nine in each of the other two. In the first ten years 19 cases were seen, all in the second half of the year, most in September–November, and nearly all were of types 1 and 2; from 1931–34, types 3 and 4 predominated and cases occurred in every month of the year except July, most in May. The article is illustrated with charts of cases and with a map showing the distribution in Cyrenaica. H. H. S.

RHODES (W. F.). **Typhus-like Fevers in the Union of South Africa.**—*South African Med. Jl.* 1934. Nov. 10. Vol. 8. No. 21. pp. 797–799.

The author refers to the three types of typhus which are known to occur in South Africa:—

1. *Epidemic type.*—This may be very severe and fatal in the native population, occurs in the winter and is louse-borne. The Weil-Felix reaction is positive, in some cases in high dilution up to 1/20,000.

2. *Tick bite fever.*—Tick-borne with primary sore and adenitis. Weil-Felix reaction positive but not noted till about 4th week, *i.e.*, in convalescence. XK also agglutinated.

3. *Endemic type.*—Occurs in the summer, not due to lice, probably due to rat flea. Weil-Felix reaction noted as early as 6th day and up to a dilution of 1/4,000. D. H.

PIJPER (Adrianus) & **DAU** (Helen). **South African Typhus.**—*Jl. Hygiene.* 1935. Feb. Vol. 35. No. 1. pp. 116–124. With 2 figs. [29 refs.]

In 1933–34 some 40 cases of sporadic or endemic typhus occurred in Pretoria and were investigated by the authors. The majority of the cases were mild but one or two patients were severely ill with all the symptoms of classical typhus. There was no evidence of contact infection and lice and ticks could be definitely excluded as vectors of the disease.

The Weil-Felix reaction was carried out in 30 cases, OX19, OX2 and OXK emulsions being employed; all 3 varieties were agglutinated but in varying degree. The most interesting feature of the results was that X19 and X2 were on the whole agglutinated in higher dilution than OXK and OX2 reacted at least as well as OX19.

Five cc. of blood taken from a patient at the height of fever was inoculated intraperitoneally into a guineapig and fever followed; this virus was passaged in guineapigs; occasional swelling of the testicles was noted and other symptoms of typhus infection. This virus was compared and contrasted with the viruses of tick bite fever and louse borne typhus fever.

The new Pretoria virus immunizes against itself and against the virus of tick bite fever but not against the virus of louse borne typhus (S.A.). Also the virus of tick bite fever did not immunize against the Pretoria virus whereas the virus of louse borne virus did protect against the new virus. The virus isolated from these cases of sporadic typhus was compared with a virus previously isolated from rats in Potchefstroom and the conclusion is that they are identical. 17 sera of cases of louse borne typhus were tested against the 3 varieties of *Proteus* X19, X2 and XK. Although the reactions were somewhat indefinite yet all 3 varieties were agglutinated and again X2 in as high dilution as X19, contrary to what usually occurs in European classical typhus. D. H.

SEREFETTIN (O.). La fièvre exanthématique murine à Istanbul. [**Murine Typhus at Istanbul.**—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 831-833.]

Severe epidemics of true typhus occurred in Turkey during the war and this disease is still met with. Recently cases of boutonneuse fever have been described; and in the present paper the writer records the first two cases of endemic or murine typhus in the country. The clinical symptoms were typical of this disease and the Weil-Felix reaction was positive for X19 in both cases. Guineapigs inoculated with the blood of one of the cases reacted with fever and typical orchitis.

Turkey may now be added to the countries where flea-borne typhus occurs. D. H.

RAGIOT (Ch.) & DELBOVE (P.). Typhus endémique bénin en Cochinchine. [**Endemic Typhus in Cochinchina.**—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 881-889.]

In 1908 typhus fever (classical) was described by YERSIN in Indo-China and in 1921 an epidemic of this disease occurred in Hanoi. One case of tsutsugamushi disease has recently been fully reported, and in this paper several cases of endemic typhus are described. The clinical features were as usual except for the fact that bronchopneumonia was present as a complication in most of the cases (see SACHS, below). There were no deaths.

The Weil-Felix reaction in two of the cases was as follows:—

X19 (Metz)	X19 (Syria)	XK
1/500	1/500	1/300
1/500	1/500	Nil.

All 3 varieties of *Proteus* X were agglutinated but X19 in higher dilution than XK. No primary sore was ever detected. D. H.

OZAKI (Y.) & OHTSUKA (I.). **Epidemiological Observation on the So-called "Manchuria Fever" in the City of Hsinking, Manchoukuo, in 1933.**—*Jl. Oriental Med.* 1935. Feb. Vol. 22. No. 2. [In Japanese pp. 319-332. With 2 figs. [14 refs.] English summary pp. 26-27.]

One hundred and twenty-four cases of "Manchurian fever" (typhus) were investigated, the majority in Japanese. Typical Rickettsia were found in house rats and rat fleas caught in the houses of patients and also, it is stated, an intermediate type of the virus in body lice.

D. H.

ZINSSER (Iians). **Varieties of Typhus Virus and the Epidemiology of the American Form of European Typhus Fever (Brill's Disease).**—*Amer. Jl. Hyg.* 1934. Nov. Vol. 20. No. 3. pp. 513-532. [14 refs.]

This paper is an amplification of the shorter paper by the same writer which is summarized on page 154 (above). The first part is devoted to a discussion of the two typhus viruses, human and murine, and the author points out that although there are many points of resemblance yet they are not identical but are separate varieties or types of the typhus virus.

He has carefully investigated three strains of virus isolated from cases of Brill's disease in Boston and has found that all definitely belong to the human type.

A very thorough epidemiological survey of Brill's disease has been carried out in New York and in Boston and it has been established that 94.8 per cent. of the cases have occurred among immigrants from European countries where typhus fever is epidemic or endemic; at least 90 per cent. of these people were Polish Jews. The interesting points concerning Brill's disease as originally observed by Dr. BRILL himself and confirmed by the present investigation are that the disease is a mild form of typhus, that it does not spread by contact and that it is not carried by lice; to these points can now be added that the disease is apparently not occupational and is not carried by the rat flea.

It has been definitely established recently that the endemic typhus fever of the Southern States of North America and of Mexico is carried to man by the rat flea and that the rat is the reservoir of the virus. Zinsser is of opinion that Brill's disease is different and that the reservoir of the virus in this disease is man himself; Brill's disease he considers is the result of recrudescences of infections with the human virus, the original infection having been acquired in Europe. Many of the people who developed Brill's disease in New York had been from 10 to 30 years in the City.

[It is not clear whether it is suggested that these people had had definite attacks of fever in Europe or were infected without developing fever, the virus remaining latent without producing a lasting immunity, and the disease developing when this partial immunity broke down.]

D. H.

- BAKER (J. N.), MCALPINE (James G.) & GILL (D. G.). **Endemic Typhus.**—*Amer. Jl. Public Health.* 1934. Oct. Vol. 24. No. 10. pp. 1068-1073. [16 refs.]
- , — & —. **Endemic Typhus in Alabama.**—*Public Health Rep.* 1935. Jan. 4. Vol. 50. No. 1. pp. 12-21. With 1 fig. [13 refs.]

These papers open with a discussion of the typhus problem from the historical and epidemiological point of view. They deal with the history of typhus in Alabama.

Endemic typhus was first reported in Alabama in 1922 by MAXCY and HAVENS as the result of positive Weil-Felix reactions [see this *Bulletin*, Vol. 21, p. 662]. Since then some 60 to 80 cases per year have been recorded almost entirely in the towns in the south and south eastern parts of the State ; but in 1932 there was a sudden rise to 237 cases with 11 deaths, and in 1933 some 823 cases with 35 deaths. From urban centres the disease has spread to purely rural areas. The seasonal occurrence, however, has remained constant throughout, with the summer and early autumn months accounting for most of the cases. Although the number of cases has increased, the mortality rate, about 5 per cent., has not. Much of the mortality is in the older age groups ; a contributing factor being a concurrent disease of the lungs, heart or kidneys. The Weil-Felix reaction is almost invariably positive with *Proteus* X19. Rat destruction and rat proofing of stores and houses are the measures of control recommended. D. H.

- LORANDO (N.). Les réflexes rotuliens dans le typhus endémique. [**Knee Jerks in Endemic Typhus.**]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 37-39.

The authors have tested some 10 cases of endemic typhus and in all have noted absence of knee jerks ; they suggest that this may help in the differential diagnosis from boutonneuse fever. D. H.

- HELMAN (J.). **The Use of Whole-Blood from Convalescent Cases in the Treatment of Typhus Fever.**—*South African Med. Jl.* 1934. Oct. 27. Vol. 8. No. 20. p. 760. With 2 charts.

During an outbreak of severe typhus fever patients were treated by injections of whole blood from convalescent cases, with apparent benefit.

40 cc. of blood was given intramuscularly at the first injection and 20 cc. at a later period in the fever. The treated patients showed a marked improvement in the general condition after a day or two, convalescence was rapid and no complications followed. Two charts of treated cases are given. D. H.

- VARELA (Gerardo), GAY (M. A. Parada) & AGUAYO (Manuel). Expériences avec le sérum contre le typhus exanthématique. [**Experiments with Anti-Typhus Serum.**]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 436-438.

This serum was prepared by repeated intravenous injections of a horse with emulsions of killed *Rickettsia* obtained from irradiated rats. The horses were bled and the serum concentrated. It was found to protect guineapigs against the homologous Mexican virus but not

against the European epidemic virus. It is proposed to test the serum in the treatment of cases of the disease and also as a prophylactic measure.

D. H.

CIUCA (M.), BALTEANU (J.) & CONSTANTINESCO (N.). Contribution à l'étude expérimentale du typhus exanthématique. Maladie inapparente du chat. [**Inapparent Typhus in the Cat.**].—*C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 511-513.

Cats were fed on the brain and spleen of guineapigs infected with typhus virus (blood of case of fever); no reaction was noted, no fever and no positive Weil-Felix reaction; the animals were killed after an incubation period of 6 days and emulsion of the brain inoculated into guineapigs. These animals reacted with fever and when tested later were shown to be immune to the virus.

This experiment was done on three occasions with similar results.

D. H.

KLIMENTOWA (A. A.). Les rats comme réservoir du virus du typhus exanthématique. [**Rats as Reservoir of Typhus.**].—*Arch. Sci. Biol.* 1934. Vol. 35. Ser. B. No. 2. [In Russian pp. 603-610. [20 refs.] French summary pp. 610-611.]

Fifty-four rats captured in Leningrad were killed and with emulsions made of the brain, 18 guineapigs were inoculated intraperitoneally. From one group of guineapigs a virus was isolated which produced fever in the guineapigs but without an orchitis; these animals were later immune to inoculation of rat virus but were not immune to the inoculation of the human typhus virus.

D. H.

LÉPINE (P.). Absence habituelle du typhus murin chez les souris capturées à Athènes. [**Absence of Murine Typhus from Athens Mice.**].—*C. R. Soc. Biol.* 1934. Vol. 117. No. 35. pp. 848-849.

The author has already shown that when cases of endemic typhus are occurring in a district of the town the virus of that disease can be readily isolated from rats in that district. He now finds that it is not possible to isolate the virus from mice captured at the same time and in the same district. The white rat is more susceptible to the virus of typhus than is the wild rat; and although the wild mouse is not susceptible the white mouse can be infected.

D. H.

DURAND (Roger) & HOMBOURGER (Katia). Sensibilité de la souris à un virus typhique chinois et au virus de la fièvre pourprée. [**Susceptibility of the Mouse to a Virus of Typhus from China and to the Virus of Rocky Mountain Fever.**].—*Arch. Inst. Pasteur de Tunis.* 1935. Jan. Vol. 24. No. 1. pp. 70-76. With 2 charts.

NICOLLE and others have already shown that the murine typhus can be passaged in mice practically indefinitely whereas the historic virus dies out after one or two passages. The methods followed in the present investigation were similar to those employed by NICOLLE and LAIGRET [this *Bulletin*, Vol. 30. p. 883.]

Conclusion.—The mouse is susceptible to the Chinese virus but only reacts with an inapparent infection and the virus can only be passaged once or occasionally twice; this virus therefore is a true typhus virus. Mice are highly susceptible to the virus of Rocky Mountain fever which can be passaged indefinitely in these animals. *D. H.*

KASAHARA (S.), YOSHIDA (S.) & OKAMOTO (Y.). Nachweis der Rickettsien in verschiedenen Organen der mit mandschurischen und japanischen endemischen Flecktyphusvirus infizierten Mäuse. [**Demonstration of Rickettsia in Various Organs of Mice Infected with Manchurian and Japanese Endemic Typhus Virus.**]—*Zent. f. Bakt.* I. Abt. Orig. 1935. Mar. 18. Vol. 133. No. 7/8. pp. 406–411. With 5 figs.

Three strains of virus were employed, mice were first infected from guineapigs and the virus was then passaged in mice using large doses of virulent material. The mice were killed when infected and the various organs sectioned and stained and examined for Rickettsia; these organisms were readily found not only in the tunica and omentum but also in cells in the liver, spleen, kidneys, lungs, adrenals and endocardium. These cells were peculiar in many ways and the authors call them Rickettsia cells. It was noted that the virus passaged through mice did not lose its virulence for guineapigs. *D. H.*

VAUCEL (M.) & HASLE (G.). Un cas d'affection du groupe "typho exanthématique" révélé par la maladie expérimentale du cobaye. [**Case of Fever of Typhus Group revealed by Guinea-pig Inoculation.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Jan. Vol. 13. No. 1. pp. 25–29. With 4 charts.

A soldier developed fever with marked nervous symptoms and extreme delirium. No rash, blood culture negative, Weil-Felix reaction negative. Diagnosis encephalitis; death on 8th day. Blood taken during the fever was inoculated into 2 guineapigs; after an incubation period of 4 days both developed fever with slight enlargement of the scrotum; the virus was passaged. A true typhus virus (Pekin) was obtained and two of the animals which had recovered from the fever were inoculated; both developed fever and died. It is considered, however, that the disease from which the patient died belonged to the group of typhus-like diseases. *D. H.*

BLANC (Georges) & MARTIN (L. A.). Iridocyclite expérimentale provoquée par virus typhique. [**Iridocyclitis Experimentally produced by Typhus Virus.**]—*C. R. Acad. Sci.* 1935. Mar. 4. Vol. 200. No. 10. pp. 865–867.

Inoculation of the virus of typhus and of Japanese River fever into the eye of rabbits produces a specific reaction characterized by iridocyclitis and inflammation of Descemet's membrane. In the present paper the authors show that the inoculation of the virus of murine typhus produces a similar reaction in the rabbit; also the same condition can be produced in the eye of sheep, dog, monkey and pig.

An interesting point is that the specific reaction was just as severe in the eye of the sheep, an animal not susceptible to infection with

typhus virus, as it was in the eye of a susceptible animal such as the monkey or rabbit. Another unusual finding was that when one eye of an animal had reacted and recovered, if the other eye was inoculated with the same virus, a positive reaction resulted; also if animals such as the monkey and the rabbit were immunized to the murine virus by intraperitoneal inoculation and were later tested by intraocular inoculation of the same virus, the specific reaction appeared just as it did in animals which had not been previously immunized. *D. H.*

TCHANG (J.) & LOTSONG (Simon). Les réactions sérologiques des animaux de laboratoire inoculés avec le virus du typhus exanthématique de Chine. [**Serological Reactions of Laboratory Animals inoculated with Chinese Typhus Virus.**]*—Arch. Inst. Pasteur de Tunis.* 1934. Dec. Vol. 23. No. 4. pp. 441-446.

Employing the Pekin strain of typhus virus for inoculation of animals the authors found that out of some 500 sera of guineapigs tested none gave a positive reaction with Proteus X19. Only 2 rats out of 23 inoculated gave a positive reaction but one-third of the rabbits gave positive results.

On the other hand when emulsions of Rickettsia were utilized in place of Proteus positive results in guineapigs were obtained in all cases if the sera were tested during the febrile period. Also similar results were obtained with white and grey rats and with rabbits.

D. H.

SPARROW (Hélène). Etude d'un virus typhique d'origine humaine isolé en Mongolie. [**Study of a Typhus Virus of Human Origin isolated in Mongolia.**]*—Arch. Inst. Pasteur de Tunis.* 1935. Jan. Vol. 24. No. 1. pp. 56-64.

This virus isolated from a severe case of typhus was described by Dr. GAJDOS [this *Bulletin*, Vol. 30, p. 876]. Apparently it was in some ways intermediate between a human virus and a murine virus. It was brought to Tunis by Dr. GAJDOS and studied there.

Fifty-one guineapigs were inoculated with the virus; 38 were males and of these only five showed orchitis and in two the condition was slight and transient. Rats inoculated with the virus did not develop fever and only 3 out of 12 showed a positive Weil-Felix reaction of 1/40 to 1/80. The brains of these rats taken on the 10th to 12th day after inoculation were infective for guineapigs. Rabbits inoculated with the virus did not have fever but their serum gave a positive Weil-Felix reaction up to a dilution of 1/600. The Mongolian virus protected against a Tunisian strain of true typhus, and *vice versa*.

GAJDOS and CHANG in their original paper stated that this virus produced a very marked scrotal reaction in every male guineapig tested but in a later series of inoculations the reaction appeared only in half the guineapigs inoculated and was much milder in character. As is stated above when tested in Tunis only 3 out of 38 guineapigs showed definite orchitis and the virus gave all the usual reactions of a typical human virus; (a) The fever curve in guineapigs was identical with that of the local human strain, (b) the virus could not be passaged in mice, and gave an inapparent infection in rats and rabbits; and (c)

could be and was carried by lice. For these reasons the conclusion is that the Mongolian virus is a true human typhus virus. *D. H.*

RONSE (Marguerite) & BRUYNOGHE (Guy). Au sujet de l'entretien du virus du typhus exanthématique murin. [**Maintenance of the Virus of Murine Typhus.**]*—C. R. Soc. Biol.* 1935. Vol. 118. No. 12. pp. 1258-1260.

The particular murine virus studied in this research showed certain remarkable changes during passage in laboratory animals.

When first isolated the virus was highly virulent for wild rats and also for white rats and produced fever and orchitis in guineapigs; after passage in guineapigs over a period of 18 months it was found to have lost its virulence for rats but still produced the marked effect on guineapigs.

The authors consider that these results were due not to any peculiarity in the virus itself but to the fact that in place of passaging the virus from guineapig to guineapig by the inoculation of emulsion of brain, they had employed emulsion of tunica tissue. Eighty passages were carried out in this manner. The virus had lost in virulence for the animal from which it was obtained, the rat, but had gained in virulence for the animal, the guineapig, in which it was maintained.

D. H.

LE CHUITON (F.) & BOURGAIN (M.). Tentative de mutation d'un virus du typhus murin en virus boutonneux, par passage dans l'organisme de *Rhipicephalus sanguineus*. [**Attempt to change the Virus of Murine Typhus into Boutonneuse Fever Virus by Tick Passage.**]*—Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 825-830. With 2 figs.

It has been suggested that the virus of endemic typhus might be transformed into the virus of boutonneuse fever by passage through ticks. The authors failed in their attempt.

The authors collected male and female ticks of the species *R. sanguineus* from districts free from either endemic typhus or boutonneuse fever. The ticks were fed on a guineapig during the fever produced by the virus of endemic typhus. Later on numerous larvae were collected from these ticks; some larvae were emulsified and the emulsion inoculated into guineapigs and some were fed on guineapigs but none of the animals became infected and when tested later none showed any immunity to the virus of endemic typhus. *D. H.*

GIROUD (P.) & HABER (P.). Action de l'électropyréxie par les radiations à ondes courtes sur le cobaye infecté par un virus de typhus exanthématique. [**Effect of Short Wave Radiotherapy on Typhus in Guineapigs.**]*—C. R. Soc. Biol.* 1934. Vol. 117. No. 31. pp. 407-409. With 1 chart. Also in *Arch. Inst. Pasteur de Tunis.* 1935. Jan. Vol. 24. No. 1. pp. 84-85.

No effect whatever was noted on the course of the fever in treated guineapigs. But as the virus survived longer in treated than in untreated animals it is suggested that the action on the tissues had interfered with their resistance. *D. H.*

KRONTOWSKY (A. A.), JAZIMIRSKA-KRONTOWSKA (M. C.), SAVITSKA (H. P.) & SOLITERMAN (P. L.). Application de la méthode des cultures de tissus à l'étude du typhus exanthématique. V. Nouvelles expériences de culture du virus du typhus exanthématique par de nouveaux procédés. [**Culture of Typhus Virus by New Method.**]*—Ann. Inst. Pasteur.* 1934. Dec. Vol. 53. No. 6. pp. 654-663. With 8 charts. [29 refs.]

In previous tissue culture experiments the authors note that the tissue employed is taken from infected animals and is incubated along with healthy tissue cells. In the method of tissue culture described in this paper living tissue cells from normal animals are employed and the virus is obtained from the plasma of infected guineapigs and is added to the culture material in amount less than the minimal infecting dose.

The normal tissue cells employed were: (1) White cells from blood of guineapig; (2) Portions of the membranes of the eyes of rabbits; (3) Cells from peritoneal effusion of guineapigs. After 5 days' incubation portions of the tissue cells were removed and inoculated intraperitoneally into guineapigs and produced typical fever and the lesions of typhus infection; showing that multiplication of the virus had taken place in the healthy tissue cells in culture.

D. H.

NIGG (Clara). **On the Preservation of Typhus Fever Rickettsiae in Cultures.***—Jl. Experim. Med.* 1935. Jan. 1. Vol. 61. No. 1. pp. 17-26. [20 refs.] [Summary appears also in *Bulletin of Hygiene.*]

The author observed that, while tissue cultures of murine rickettsiae in a serum-Tyrode mixture remained alive and virulent for several months at 37°C. and -20°C., they generally died out in a week or two at the intermediate temperatures of 20°C. and -4°C. Evaporation of water and escape of gas were prevented by sealing the flasks with paraffined rubber stoppers. It was not only stock strains that remained alive in culture at a suitable temperature for so long; first generation cultures also remained virulent for at least 15 weeks at 37°C. Likewise, typhus-infected tissues, such as minced guineapig tunica, remained infective for at least 10 weeks at 37°C. when suspended in a serum-Tyrode mixture.

G. S. Wilson.

DAVIS (Gordon E.). **The Weil-Felix Reaction in Experimental Rocky Mountain Spotted Fever and Certain Other Typhus-like Diseases.***—Public Health Rep.* 1935. Mar. 22. Vol. 50. No. 12. pp. 404-412. [17 refs.]

FELIX has shown that if a passage virus of one of the typhus group of diseases is inoculated into rabbits "main" agglutinins are produced for the variety of Proteus X associated with that virus, but a second inoculation of the same virus does not produce stimulation of these agglutinins whereas a later inoculation of a heterologous virus into the same animal produces agglutinins for the variety of proteus associated with that virus.

Following up this suggestion the author has inoculated groups of rabbits intraperitoneally with guineapig passage virus of one of the typhus-like diseases and later with another.

The viruses employed were :—(1) Rocky Mountain spotted fever. (2) São Paulo exanthematic typhus. (3) Endemic typhus (United States). (4) Boutonneuse fever.

The Proteus X varieties utilized were OXK, OX2, HX2 and OX19.

Results.—All of the group of six rabbits inoculated with the São Paulo virus and subsequently with the virus of Rocky Mountain spotted fever gave a positive reaction with OX19, and OX2 after the first injection and no reaction after the second ; when the order of injection was reversed the result was the same.

Of 10 rabbits injected with the virus of spotted fever and subsequently with the virus of boutonneuse fever all gave a positive reaction with OX2, OX19 or both after the first injection and none after the second.

Of 24 rabbits inoculated with the virus of boutonneuse fever and subsequently with the virus of spotted fever all were essentially negative following the first injection and only four were positive after the second.

Six rabbits inoculated with the virus of endemic typhus gave a positive reaction with OX19 but the results were negative after the subsequent injection of spotted fever virus although all the animals were infected. When the viruses were injected in reverse order all animals gave a positive reaction with OX2 following the injection of spotted fever virus while only OX19 agglutinins appeared after the later injection of endemic typhus virus.

The interesting points brought out are that following injection of São Paulo or Rocky Mountain fever virus into rabbits X2 agglutinins are present even more regularly than X19 agglutinins. The author claims that this is the first record of the presence of X2 agglutinins in significant titre in rabbit sera following infection with any of the typhus viruses ; but see paper by PIJPER and DAU [*ante*, p. 154].

The results of the agglutinin experiments suggest the immunological identity of the viruses of São Paulo typhus and Rocky Mountain fever and the close relationship but not identity of the virus of boutonneuse fever with these viruses.

D. H.

BLANC (Georges) & GAUD (Maurice). La vaccination contre le typhus exanthématique au Maroc. Premières applications de la méthode par vaccin vivant bilité. [**Vaccination against Epidemic Typhus in Morocco. First Use of a Living Vaccine attenuated by Ox Bile.**]*—Bull. Acad. Méd.* 1935. Apr. 2. 99th Year. 3rd Ser. Vol. 113. No. 13. pp. 407–419. With 3 figs.

The virus employed had been isolated from rats in Casablanca and passaged in guineapigs ; it was known to give only a very mild attack of fever in man [*ante*, p. 163].

The experiment was divided into 3 categories.

1. Inoculation of 723 men in a penitentiary where all were healthy and there was no typhus.
2. Inoculation of 850 men, women and children in an infected locality where lousing had already been carried out.
3. Inoculation of 607 persons in an infected population where no lousing had been done.

A total of 2,180 persons was inoculated. There were no severe reactions in any of the inoculated and in both the infected localities the disease was checked.

D. H.

KLIGLER (I. J.) & ASCHNER (M.). **Immunization of Animals with Formolized Tissue Cultures of *Rickettsia* from European and Mediterranean Typhus.**—*Brit. Jl. Experim. Path.* 1934. Dec. Vol. 15. No. 6. pp. 337-346. With 3 charts. [17 refs.] [Summary appears also in *Bulletin of Hygiene.*]

Tissue cultures of *Rickettsia* were put up with guineapig tunica, guineapig serum, and Tyrode solution. The inoculum with the European virus was infected louse guts, with the rat virus infected guineapig tunica tissue. The cultures were incubated at 28°-30°C. For preparation of vaccine 2-3 week old cultures were generally used. A thorough suspension of the material was obtained by grinding, freezing and thawing, and 0.1 per cent. formol was added. This vaccine was found to be sterile and non-infective even in large doses. Experiments made on a small number of guineapigs seemed to show that it was possible to protect against subsequent infection with living *Rickettsia* provided at least three fairly large doses were given. Rabbits inoculated repeatedly with the vaccine developed a positive Weil-Felix reaction. The authors conclude that successful immunization with killed *Rickettsia* is mainly a question of adequate dosage.

G. S. Wilson.

LAIGRET (Jean) & DURAND (Roger). **Essais négatifs d'atténuation des virus typhiques par le vieillissement. [Negative Attempts at Attenuation of Typhus Virus by Aging.]**—*Arch. Inst. Pasteur de Tunis.* 1935. Jan. Vol. 24. No. 1. pp. 77-83.

By "vieillissement" is meant the retention of the virus in an incubator or room at a temperature of 20°C. for 2 or 3 days. This method has already been successfully employed in the preparation of vaccines from the viruses of rabies and yellow fever. "Desiccation" as employed in preparation of rabies vaccine is of little use; it is the time and temperature in the process that cause attenuation of the virus.

Two typhus viruses were used in the present investigation, a human virus and a rat virus. Emulsions of the brain of infected guineapigs and rats were made in glycerine and exposed to a temperature of 20°C. for 2 to 4 days and attempts were then made to immunize normal guineapigs without producing symptoms of disease. Results were negative and the authors state that this method cannot be utilized for the preparation of typhus vaccine.

D. H.

MASAYAMA (Suguru). **Experimentelle Untersuchung ueber den Uebertragungsmechanismus von Flecktyphus- und Fleckfieber-Virus durch die Kleiderlaus. [Experimental Research on the Method of Infection by Lice in Typhus.]**—*Jl. Oriental Med.* 1935. Jan. Vol. 22. No. 1. [In Japanese pp. 177-205. With 1 text fig. & 6 figs. on 1 plate. [16 refs.] German summary pp. 15-16.]

The author states that it is not yet quite clear how typhus virus is carried by lice from the sick to the healthy. He describes his investigations, which, however, do not seem to add anything material to what is already known.

D. H.

BLEWITT (Basil). Review of Fevers of the Typhus Group (Vector Unknown) occurring at Ahmednagar during 1933.—*Jl. Roy. Army Med. Corps.* 1934. Nov. & Dec. Vol. 63. Nos. 5 & 6. pp. 313-319; 379-387. With 3 figs.

In Ahmednagar during 1931 there were no cases of fevers of the typhus group reported; in 1932 there were 8 and in 1933, 13. All occurred in the months September to December inclusive, a definite seasonal incidence; during these months the cases were strictly limited to areas which had certain features in common, viz., the presence of water, mango trees, rank grass and tick infested buffaloes.

In one case, which occurred in a child in a bungalow in the cantonment, the grazing in the compound had been let for the first time and buffaloes were grazed there for some days before the child was taken ill. Out of 13 cases investigated, however, only two were able to state definitely that they had been bitten by ticks, which they had removed from their bodies; in one case fever followed 15 days later, in the other 18 days after the tick bite; the ticks were not seen by the author.

A very careful description of the clinical course of the disease is given. The fever lasted about 14 days and was severe, resembling boutonneuse fever, apart from the fact that a primary sore was never detected. Photographs show the appearance and distribution of the rash. In the opinion of the author the macular rash occurs early on the soles but owing to the thickness of the skin is not detected; later the petechial form of the rash appears and is readily seen. There were no fatal cases in the series and all made a rapid convalescence.

Laboratory investigations.—Blood cultures taken early in the fever were all negative and in 50 per cent. of the cases the peripheral blood showed a slight polynuclear leucocytosis. In some of the inoculated men there was a slight rise of the agglutinin for *Bact. typhosum* during the course of the fever. The Wassermann and Kahn reactions were negative in all cases in the first week, but 75 per cent. gave a positive reaction in the 3rd week and 80 per cent. in the 4th week; all, however, were again negative by the 6th week. As regards the Weil-Felix reaction a dilution of 1/125 was taken as a base line and anything over this as definitely positive, especial note being made of a rising titre. Sixty per cent. of the cases gave a positive reaction during the 2nd week and 100 per cent. were positive during the 3rd week; the highest titre obtained was 1/500.

Three strains of *Proteus* X were employed; X19 was agglutinated in highest dilution, X2 being next and XK least, but this strain was also agglutinated.

D. H.

i. **SACHS (Albert). Notes on Seven Cases of the Indian Typhus-like Fevers.**—*Jl. Roy. Army Med. Corps.* 1935. Mar. Vol. 64. No. 3. pp. 163-173. With 7 charts & 5 figs.

ii. **MACNAMARA (C. V.). An Epidemic of Typhus (Vector Unknown) in the Simla Hills.**—*Ibid.* pp. 174-183. With 1 map.

i. Seven cases of typhus are described, occurring at the stations of Jubbulpore, Bareilly and Peshawar. Two of the seven gave a history of tick bite and one of these proved fatal.

Careful notes are given of this fatal case; death was due to double bronchopneumonia with hyperpyrexia. There was nothing characteristic in the post-mortem appearances which were those of many acute

infections. *Rickettsia* was not found in the tissues but round-celled infiltration and arteriolitis were noted in the liver. The rash in this case was definitely petechial. In the other cases the rash was maculopapular involving the face and the palms and soles and was very marked; photographs are given. All the patients developed inflammation of the bronchi followed by pneumonia. The pulse was slow in relation to the temperature.

Laboratory findings.—Blood cultures taken on the 4th to the 6th day were all negative. Widal reaction, a sympathetic rise in the H agglutinins for *Bact. typhosum*, was noted. In the fatal case, death on the 11th day, the Weil-Felix reaction was only positive, 1/50, for OX19. In cases 3 and 4 HX19 was agglutinated in a dilution of 1/250 and 1/1,000. Case 5 gave the following results:—

	7th day	10th day	17th day
OX19	nil	1/250	1/500
OXK	nil	nil	nil

ii. There is no record of this disease in the Simla Hills before 1932 in which year there were 5 cases with 2 deaths. In the present epidemic, 1934, there were 15 cases; all occurred in the period just before the rains, August–September–October, ceasing when the rains broke. Nothing could be discovered as to the vector and in no case was there any history or trace of insect bite. It has been suggested that the Indian squirrel, recently introduced into the district, may be a reservoir.

Clinical.—Onset sudden, severe headache was practically the only symptom complained of, flushed face, injected conjunctivae, pulse slow in relation to the temperature, which was high. The rash appeared on the 5th day and consisted of blotchy macules. The serum of all the cases agglutinated emulsions of OXK in high dilution ranging from 1/150–1/250,000 with a rising titre. [This is the first series of cases of the disease in India in which definite agglutination results have been obtained.]

[It is interesting to compare these two series of cases, the one occurring in the Hills, the other in large stations in the plains of India. In the one series (Macnamara) the disease was mild although the fever was high and prolonged, the rash was faint and ill-defined and the only symptom was severe headache. All the sera agglutinated OXK, some in as high a dilution as 1/250,000. In the other series (Sachs) the cases were severe with lung complications and a very definite and obvious papular and in the one case (fatal) petechial rash. The sera of the cases in this series agglutinated X19 in low dilution but did not agglutinate OXK.]

D. H.

BOYD (J. E. M.). *Indian Typhus: a Patient's Views.*—*Jl. Roy. Army Med. Corps.* 1934. Dec. Vol. 63. No. 6. pp. 394–398.

Colonel Boyd who is a keen entomologist and trained clinician, himself suffered from the disease, cases of which he had already had the opportunity of observing in his hospital. He notes that it differs from true typhus in that there is no stupor nor delirium, nor oedema of the face and the mortality is nil. As regards the vector lice could be

definitely excluded and in the cases observed by him and in his own case there was no record of tick bite; as he says "we one and all denied any knowledge of having been bitten by ticks." [In other countries similar diseases may be conveyed by the larval form of the tick which is of minute size and may readily escape detection; the bite may be painless.]

In his own case Colonel Boyd noted that the staining of the skin following the rash was still visible six months after the fever had ceased; he also points out that the severe headache and toxæmia render the patient disinclined to take nourishment and those in charge should see that suitable fluid diet is provided and that it is consumed; otherwise convalescence may be prolonged owing to the patient's weakness.

D. H.

ROBERTS (J. Isgaer). **The Ticks of Rodents and their Nests, and the Discovery that *Rhipicephalus sanguineus* Latr. is the Vector of Tropical Typhus in Kenya.**—*Jl. Hygiene*. 1935. Feb. Vol. 35. No. 1. pp. 1-22.

Part I of this paper deals with ticks in relation to rodents and their nests in Kenya.

It had been suggested that plague and plague immunity in rodents may be connected with tick infestation but this suggestion was not confirmed by investigations. The common ticks found on rodents and in their nests are the larval stages of *Haemaphysalis leachi* and *R. simus* neither of which attack man although the former is often found on dogs, cattle and game.

Part II is concerned with the rôle of *Rhipicephalus sanguineus* as the vector of typhus in Kenya.

The commonest form of tick on man in and around Nairobi and in the endemic typhus centres is not *R. sanguineus* but *R. pulchellus*; any one walking through long grass in pursuit of game or in the "rough" on the local golf course is bound to pick up many of these ticks and the bite of the larval form gives rise to small ulcers and in one case this was the tick removed from the site of a primary sore in a case of typhus. Numerous experiments were carried out by emulsifying *pulchellus* ticks and injecting the emulsion into guineapigs but all were negative.

R. pulchellus although common in the grass is rarely found on dogs or in houses, whereas it has been observed that *R. sanguineus* is what might be described as a "house" tick and at certain seasons of the year large numbers can be found in the woodwork of houses, common hiding places being behind the picture rails and in the frames of wooden chairs; the houses where these ticks are found are "doggy" houses. An investigation revealed that 100 per cent. of houses in which dogs were kept were infested by *R. sanguineus*. Ticks were collected from houses where cases of typhus had recently occurred, emulsified and injected into guineapigs; fever, swelling of the scrotum and other symptoms of typhus infection resulted. It is therefore concluded that the vector of tropical typhus in Kenya is the dog tick *R. sanguineus* which infests the houses in that country and that the disease is similar to *fièvre boutonneuse* in its clinical symptoms and in its etiology.

It is recommended that houses should be disinfested by means of the blow lamp and furniture by fumigation.

D. H.

CANNAVO (Letterio). Ricerche sul virus bottonoso siciliano. [**The Virus of Boutonneuse Fever in Sicily.**—*Riforma Med.* 1934. Nov. 24. Vol. 50. No. 47. pp. 1799–1804. With 2 figs. [18 refs.]

The author collected ticks (*Rhipicephalus sanguineus*) from dogs roaming about Palermo. These ticks he washed repeatedly, first with a weak solution of corrosive sublimate and then with physiological saline; he then triturated them with more saline and injected the emulsion into the glutei of a Capuchin monkey (*Cebus*). A febrile condition resulted and the serum of the animal acquired agglutinins for *Proteus* X19; it recovered.

Blood was taken into citrate at the height of the fever and was injected intraperitoneally into guineapigs. These in turn became febrile and died in about a month. At autopsy granule formation was marked in the liver, but abundant also in the lungs and elsewhere, shown by microscope to be necrotic in nature. There was also a testicular reaction, but *Rickettsia* were not discovered there. The bouton-neuse fever of Sicily which has been notified from various Provinces—Previtera, Bongiovanni in Catania; Ingrao and Scaturro in Agrigento; Gulino and Cannavò in Palermo, etc.—is, the author states, due to this virus and that cases are not more common is explained by the fact that these ticks rarely bite man.

H. H. S.

GIORDANO (Mario). La febbre esantematica del Littorale Mediterraneo in Tripolitania. [**Boutonneuse Fever in Tripolitania.**—*Arch. Ital. Sci. Med. Colon.* 1935. Mar. 1. Vol. 16. No. 3. pp. 161–185. With 1 folding map. English summary (3 lines).

This is a "congress" paper giving a general review of the subject of bouton-neuse fever in Tripolitania. The author gives detailed accounts of 20 cases, 14 adults and 6 children between 1½ and 9 years of age, dating back to 1913.

One patient's serum gave a positive Weil-Felix reaction and this, it is stated, was probably a case of Brill's disease; the rest proved negative during the course of the illness and in convalescence, although 11 strains of *Proteus* were tested. Sera from 6 out of 11 dogs from places where cases had occurred reacted positively. It is worthy of note that inoculation of emulsion of rats' brains and of triturated *Hippobosca* caught on dogs in the house of one of the patients gave positive results in guineapigs and rabbits. A spot map shows the distribution of 16 of the cases: 8 occurred in Tripoli itself and 8 outside the town.

H. H. S.

CAMINOPETROS (J.), CONTOS (B.), PHELOUKIS (T.) & PAGONIS (A.). Action curative dans la fièvre boutonneuse d'un sérum expérimental de cheval préparé. [**Curative Action of Serum prepared from Horse in Boutonneuse Fever.**—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 22–30. With 6 figs. & 3 charts.

A serum was prepared from horses by inoculation of an emulsion of infected ticks intradermally and into the conjunctiva. By both routes a local reaction resulted and fever followed. One horse received 52 and the other 23 inoculations at intervals of 15 days. The animals were then bled. Five cases of bouton-neuse fever were treated by

means of this serum ; its administration had a marked effect on the course and severity of the disease ; in place of the usual 12 days fever in untreated cases the fever ceased on or about the 7th day.

Two cases of endemic typhus were treated with the serum but its administration had no effect whatever. D. H.

AUGIER (P.) & COSSA. Syndrome d'encéphalite avec rigidité pallidale au cours d'une fièvre boutonneuse méditerranéenne. [**Encephalitis with Pallidal Syndrome in Boutonneuse Fever.**]*—Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Mar. 18. 51st Year. 3rd Ser. No. 9. pp. 432-436.

A very severe case of boutonneuse fever characterized by encephalitis with marked and painful general spasm of the muscles and pain in the joints. In this case the central nervous system was the seat of the attack of the virus. D. H.

LOMBARDO (Fortunato). Esperienze sulla presenza del virus tifico esantematico del Mediterraneo nei cani. [**The Virus of Mediterranean Typhus in Dogs.**]*—Ann. d'Igiene.* 1935. Jan. Vol. 45. No. 1. pp. 1-6. [14 refs.]

The author tested the sera of 50 dogs in Messina for their agglutinating activities with Proteus X19. Thirty-one agglutinated in dilution of 1 : 25 or over, thirteen in 1 : 50, seven in 1 : 100 and four up to 1 : 200. Ticks caught on these dogs were triturated and injected into guineapigs and produced a febrile reaction and in some cases enlargement of the spleen. Human cases of the disease, states the author, are not found in the Commune. H. H. S.

KIAN (Loe Ping). Twee gevallen van tropical ("shop") typhus bij Chineesche kinderen. [**Two Cases of Shop Typhus in Chinese Children.**]*—Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Mar. 5. Vol. 75. No. 5. pp. 447-464. With 2 figs. [31 refs.] English summary.

The following diseases caused by Rickettsia are known in the Dutch Indies : "pseudotyphus" (Schüffner) or Sumatra mite fever (van Driel) and tropical typhus W and K variety. The K type (scrub typhus) is predominant in Malacca and on the East Coast of Sumatra but in Java the W form (shop typhus) seems to be more common.

The two forms of tropical typhus can be readily differentiated by means of the Weil-Felix reaction. In the opinion of the author a positive reaction with Proteus X strains has value if the following requirements are met with.

(1) The agglutination with alcohol suspensions of Proteus X strains should be positive.

(2) There should be a rising titre of agglutination during the illness.

(3) When living motile Proteus X strains are employed the agglutination should be only of the granular (O) type and if the serum is heated to 65°C. for one hour the reaction should be negative.

Two cases of typhus in children are described. X19 was agglutinated and the fevers were diagnosed as shop typhus (W variety).

D. H.

O'CONNOR (M. P.). **The Marris Atropine Test in Tropical Typhus.**—*Malayan Med. Jl.* 1934. Dec. Vol. 9. No. 4. p. 204.

The Marris test was largely employed in the diagnosis of typhoid fever during the war. The author employed this test in 12 cases of scrub typhus and in 10 a positive reaction was obtained.

In a healthy person the injection of 1/33 of a grain of atropine results in a rise in the pulse rate of 15 beats per minute or more. In typhoid fever no such rise takes place. [See this *Bulletin*, Vol. 9, p. 466, and Vol. 11, p. 432.] *D. H.*

LEWTHWAITE (R.) & SAVOOR (S. R.). **Tropical Typhus (Rural Type) and the Tsutsugamushi Disease as encountered in the Federated Malay States. The Isolation and Maintenance of Strains of these Two Diseases in the Rabbit by the Intraocular Inoculation of Virus ; and the Demonstration of Cross-Immunity between these Two Strains.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 249–257.

The paper deals with the relationship of the virus of the rural form of tropical typhus to that of tsutsugamushi fever as it occurs in Malaya.

In 1925 FLETCHER showed that there were two types of "tropical typhus" in Malaya which he called the urban and the rural types ; it was suggested that the vector of the rural type might be a larval tick. Since then a few cases of tsutsugamushi fever with a definite primary sore and bubo have been described, the vector in this case being a mite, *T. deliensis*. The serum of the "rural typhus" cases and the tsutsugamushi cases agglutinates the K variety of Proteus OXK and the serum of the urban typhus cases the W variety of OX19. The rural type of typhus and tsutsugamushi disease resemble one another so closely clinically, apart from the presence of the primary sore in the latter, that FLETCHER suggested later that in this disease also the vector might be a mite and not a tick.

The authors have demonstrated cross immunity between rural typhus and tsutsugamushi.

In this investigation the authors used rabbits as experimental animals and inoculated the virus (defibrinated blood of cases of fever taken as early as possible) into the anterior chamber of the eye, a method employed by Japanese workers in investigating tsutsugamushi disease in Japan. The specific reaction which follows, after an incubation period of 4–15 days, consists in circumcorneal injection, inflammation of the iris and turbidity of the aqueous humour. Two strains of the virus of tsutsugamushi fever were used and four of the virus of rural typhus. It was found that the homologous strains protected against reinoculation in the sound eye with the same strain of virus and also that the virus of tsutsugamushi fever protects rabbits against the virus of rural typhus and *vice versa*, i.e., complete positive crossed immunity.

Also rabbits which had been inoculated intraperitoneally with the virus of rural typhus or the virus of tsutsugamushi developed agglutinins for OXK in their serum in dilution up to 1/500. The development of these agglutinins in the rabbits' sera is often delayed and the highest estimations were not obtained till the 60th day after inoculation. Typical Rickettsia bodies were found in smears from the

membranes of the eye in infected animals, but only in small numbers in some cases; these findings were identical in each case. *D. H.*

KAWAMURA (R.), IMAGAWA (Y.) & ITO (T.). The Well-Felix Reaction in Tsutsugamushi Disease and its Relation to Endemic Typhus in Manchukuo and Formosa.—*Kitasato Arch. Experim. Med.* 1935. Jan. Vol. 12. No. 1. pp. 26-57. With 2 charts. [25 refs.]

Most of this paper is taken up in refuting the statement, made some years ago, that tsutsugamushi fever and the K type of tropical typhus can be differentiated by the results of the OXK agglutination reaction. This standpoint has already been abandoned by workers in Malaya.

The authors find that the sera of healthy persons does not agglutinate OX19 or OX2 but that OXK may be agglutinated up to 1/100. In 38 persons suffering from various diseases, especially gonorrhoea and suppurative disease, OXK was agglutinated up to a dilution of 1/200 and in two cases 1/400. It is added that the OXK reaction in tsutsugamushi disease may remain positive for several years after the fever.

Forty-nine sera of tsutsugamushi fever cases were examined, 13 during the febrile period; all were negative to OX19 and OX2 but positive with OXK; 6 cases were found to have a titre over 1/1,600 and one as high as 1/25,000.

Sera from cases in Formosa and Boko Island were also tested and gave positive reactions to OXK up to 1/800. The Japanese cases gave the highest reaction, those from Boko the next and those from Formosa the lowest.

The primary sore is constantly present in patients in Japan Proper, but is often absent in Formosa and East Indies. *D. H.*

NICOLLE (Charles) & SPARROW (Hélène). Quelques expériences sur le virus de la fièvre fluviale du Japon (Tsutsugamushi). [**Experiments on Tsutsugamushi Virus.**]—*C. R. Acad. Sci.* 1934. Dec. 10. Vol. 199. No. 24. pp. 1349-1351.

The authors obtained the virus of Japanese River fever from Japan and have maintained it in the laboratory by passage in rats, in which the virus produces an inapparent infection.

In monkeys the virus produced a fever similar to that of typhus; one monkey out of 11 died. Only a few of the guineapigs inoculated developed fever and none died. None of the rabbits inoculated developed fever but the blood of the animals was infective for monkeys. Inoculation of the virus into the eye of the rabbit produced a typical local reaction and Rickettsia was readily demonstrated in the cells of the membranes of the eye. The serum of some of the infected monkeys agglutinated *Proteus* OXK and not OX19.

Lice were fed on monkeys during the fever; the virus was viable in these insects for 7 days but their bite was not infective. The virus was found to survive in fleas (*X. cheopis*) for 11 days and to be transmissible by their bite. *D. H.*

KOUWENAAR (W.) & WOLFF (J. W.). Experimental Sumatran Mite Fever in Guinea-Pigs.—*Jl. Infect. Dis.* 1934. Nov.-Dec. Vol. 55. No. 3. pp. 315-327. With 2 figs. [20 refs.]

Sumatran mite fever was described for the first time in the year 1908 by SCHÜFFNER under the name "pseudo typhus of Deli."

The fever in this disease usually resembles that of typhoid fever but an initial sore, similar to that in Japanese River fever and boutonneuse fever, is invariably present and is accompanied by lymphangitis. The death rate in the Javanese is about 5 per cent. but in Europeans about 40 per cent. SCHÜFFNER on the analogy of tsutsugamushi disease suggested that the disease might also be carried by a mite and in 1923 WALCH identified this mite as *Trombicula deliensis*, a species closely related to *T. akamushi*.

Clinically it is not possible to separate Sumatran mite fever from tsutsugamushi disease; the authors therefore attempted to differentiate the diseases by means of animal experiments. It was found that the virus of Sumatran mite fever produced a mild fever in monkeys with a primary papule at the site of injection, but a very severe and often fatal disease in guineapigs (63 per cent. mortality); exactly the opposite occurs with the virus of tsutsugamushi disease—a mild non-fatal infection is produced in guineapigs and a severe and fatal infection in monkeys.

D. H.

WOLFF (J. W.) & KOUWENAAR (W.). Onderzoekingen over de Sumatraansche mijtekoorts. V. [**Sumatran Mite Fever. V.**—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1934. Nov. 20. Vol. 74. No. 24. pp. 1608–1618. With 5 figs. on 1 plate. [12 refs.] English summary.

KOUWENAAR (W.) & WOLFF (J. W.). Onderzoekingen over Sumatraansche Rickettsiosen. VI, VII & VIII. [**Investigations of Sumatran Rickettsias. VI, VII & VIII.**—*Ibid.* Dec. 4. No. 25. pp. 1659–1670. With 3 figs. on 1 plate & 1 graph. [14 refs.]; 1935. Jan. 8 & 22. Vol. 75. Nos. 1 & 2. pp. 34–38. With 2 graphs & 1 plate; pp. 117–123. English summaries.

V. Infectieproeven op witte muizen. [**Experimental Infection of White Mice.**]

White mice have been proved to be very susceptible to the virus of Sumatran mite fever; nearly 100 per cent. of the infected animals died. A description is given of the symptoms noted in the mice and of the post-mortem changes. The mean duration from the time of infection to the death of the animal was 11 days. The principal changes seen post-mortem were haemorrhagic inguinal glands, enlarged spleens, small-celled infiltration between the liver cells and sometimes an exudate in the pleural and peritoneal cavities. Rickettsia could always be detected in smears from peritoneum, pleura or omentum.

No difference was noted between the symptoms produced by the virus of Sumatran fever and that produced by the virus of "scrub" typhus.

VI. Een Rickettsiose uit Varkensteken. [**A Rickettsiasis from Ticks from Wild Pigs.**]

It has been suggested that ticks as well as mites may be capable of transmitting the virus of Sumatran "mite fever." [If this is so the name given is unfortunate].

Dermacentor and Rhipicephalus ticks were collected from people in areas where mite fever and scrub typhus are prevalent and also from wild pigs in the same districts. Emulsions were made of these ticks and injected into guineapigs, monkeys and rabbits. In some of these animals fever was produced and Rickettsia were found in the tissue cells

but the lesions produced were entirely different from those produced by the virus of "mite fever." The serum of some of the wild pigs agglutinated OXK up to a dilution of 1/250 but did not agglutinate OX19.

VII. Infectieproeven met mijtekoorts op *Macacus fuscatus*, de Japansche aap. [**Experimental Infection of the Japanese Monkey, *M. fuscatus*, with Mite Fever.**]

VIII. Infectieproeven met mijtekoortsvirus op hoogere apen. [**Experimental Infection of Various Monkeys with Mite Fever.**]

In previous papers the authors have recorded the results of the action of the virus of Sumatran "mite fever" on several species of monkeys. They found that the virus of this disease produces only a mild fever in monkeys without any lasting immunity, whereas the virus of tsutsugamushi fever in Japan produces a severe and often fatal illness in the species of monkey, *M. fuscatus*, employed in that country. The authors considered that these differences might be due to the fact that different species of monkeys were employed in the experiments. They therefore obtained from Japan some *M. fuscatus* and inoculated them with the local virus; exactly the same result as before resulted, namely only a mild fever and no lasting immunity; moreover one of the monkeys which had been rendered immune to the virus of tsutsugamushi fever in Japan was found to be susceptible to the virus of Sumatran mite fever. For these and other reasons the authors consider that the viruses of Japanese River fever and Sumatran mite fever are not identical. D. H.

MONTEIRO (J. Lemos). Essais de transmission expérimentale du typhus exanthématique de São Paulo par la punaise *Cimex lectularius*. [**Attempts to transmit São Paulo Typhus by *Cimex lectularius*.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 9. pp. 918–920.]

Bed bugs were infected by feeding on guineapigs during the febrile period. The conclusions are as follows:—

1. The virus of São Paulo typhus is active immediately after its ingestion by the bugs but loses its activity after the short delay of 24 hours.

2. Tests after 48 and 72 hours, 5, 10, 13, 16 and 35 days all gave negative results, whether by inoculation of excreta or the crushed up bugs, or by feeding the bugs on guineapigs.

The authors suggest that the positive results reported by MAGALHÃES were due to the use of a Mexican typhus virus and not the São Paulo virus. D. H.

MONTEIRO (J. Lemos). O "typho exanthematico de S. Paulo" e suas relações com a febre maculosa das Montanhas Rochosas, á luz das provas de imunidade cruzada. [**The Relations between S. Paulo Typhus and Rocky Mountain Fever in the Light of Cross-immunity Tests.**—*Mem. Inst. Butantan.* 1933–1934. Vol. 8. pp. 207–220. [10 refs.] English summary.]

The virus of Rocky Mountain fever for these tests was obtained from the National Institute of Health and the R.M. Spotted Fever Laboratory, Hamilton. Infected specimens of *Dermacentor andersoni* were

also received from Hamilton. The experimental animals were guinea-pigs. It was found that guinea-pigs immunized against S. Paulo typhus failed to react to R.M. fever virus obtained from infected ticks. Again, guinea-pigs recovered from R.M. fever are immune to S. Paulo typhus virus, and Dr. R. E. DYER of the National Institute of Health has communicated to the author that a monkey after an attack of R.M. fever is also immune to S. Paulo typhus virus. The author concludes that both belong to the same group "whose type infection is the Rocky Mountain spotted fever, of which it [S. Paulo typhus] may represent but a variety."

H. H. S.

TRAVASSOS (J.) & MONTEIRO (J. Lemos). Contribuição ao estudo da reacção de Weil-Felix na infecção experimental pelos virus do "typho-exanthematico de S. Paulo" e febre maculosa das Montanhas Rochosas. [**The Weil-Felix Reaction in S. Paulo Typhus and Rocky Mountain Spotted Fever.**—*Mem. Inst. Butantan*. 1933-1934. Vol. 8. pp. 57-80. With 1 graph. English summary.]

Among 60 patients suffering from S. Paulo typhus 41 or 68.3 per cent. gave a positive Weil-Felix reaction with Proteus X19. The days of the disease on which the reactions were taken are of interest. Of 24 sera examined in the first 5 days, 14 were positive (58 per cent.); between the sixth and tenth days 22 out of 36 (61 per cent.); between 11 and 15 days 20 out of 23 (87 per cent.); of 8 between the 16th and 20th days all were positive; of 9 tested later than this 7 were positive; in other words the percentage of positive reactions rose till the 20th day and then began to decline.

Experimental inoculation into rabbits of the S. Paulo virus and that of Rocky Mountain fever, showed that the serum reacted in a higher titre with R.M., but the decrease is sharper and more definite than in the case of S.P. infection; in this the decrease is more gradual. This applies to both Proteus OX2 and OX19. As regards Proteus OXK the titres giving agglutination were more irregular but more stable on the whole with S.P. infection sera. With OXL the titre of serum giving a positive is high in both infections, but decreases in the same way as with OX2 and OX19, *i.e.*, more sharply and definitely with R.M. sera.

The reaction with Proteus OXL, OX2 and OX19 differs in experimental infection from what is observed in natural human infection with S.P. virus; the titre agglutinating the two former is higher than for the third in experimental infection, the reverse occurring in human cases, while the titre for Proteus OX19 and OXL is higher than for Proteus OXK with R.M. fever sera.

H. H. S.

MONTEIRO (J. Lemos). Comportamento experimental do coelho aos virus do "typho exanthematico de S. Paulo" e da febre maculosa das Montanhas Rochosas. [**Reaction of Rabbits to S. Paulo and Rocky Mountain Fever Viruses compared.**—*Mem. Inst. Butantan*. 1933-1934. Vol. 8. pp. 39-46. With 3 graphs & 4 figs. (2 coloured) on 1 plate. English summary (9 lines).]

Intraperitoneal inoculation of the S. Paulo typhus virus into rabbits gave rise to a typical febrile reaction, but while some showed no scrotal reaction at all, others showed oedema and a slight hyperaemia which subsided in a few days. In the case of the virus of Rocky Mountain

fever similar inoculation was followed by oedema, haemorrhage and necrosis of the scrotum. The differences are such that in spite of the mutual production of immunity [dealt with elsewhere] the author is of opinion that the viruses are distinct. H. H. S.

MONTEIRO (J. Lemos). *Vaccina contra o "typho exanthematico" de S. Paulo. Novas correlações entre esta infecção e a febre maculosa das Montanhas Rochosas. [Vaccination against S. Paulo Typhus. Relations between this Disease and Rocky Mountain Spotted Fever.]—Mem. Inst. Butantan. 1933-1934. Vol. 8. pp. 9-20. With 5 graphs. [10 refs.] English summary (9 lines).*

The vaccine employed was prepared by trituration of ticks, *Amblyomma cajennense*, infected by feeding on a guineapig, itself in a febrile state from infection with S. Paulo virus. For the exact details of the preparation the original article should be consulted. This vaccine was first tested on guineapigs and found to be potent in prophylaxis. It was then tested as regards its protective properties against the virus of Rocky Mountain fever and found effective in a single dose. The reverse of this was then tried out, using Parker's vaccine for Rocky Mountain fever for its protective properties against infection by the São Paulo virus. Whereas a single dose of the first (S. Paulo vaccine) protected equally against either, two doses of the Parker's vaccine were needed to protect guineapigs against the São Paulo virus.

It was found also that these animals after being immunized against Rocky Mountain fever, if the original infection was severe, were immune also to the São Paulo typhus. H. H. S.

DA CUNHA (A. M.). *Sur la culture des Rickettsia du typhus exanthématique de São Paulo dans la membrane chorio-allantoïde de l'embryon de poulet. [Culture of the Rickettsia of São Paulo Typhus on the Membranes of the Chick Embryo.]—C. R. Soc. Biol. 1934. Vol. 117. No. 30. pp. 392-394. With 1 fig.*

Fertilized eggs were placed in an incubator at 40°C. and incubated for 7 to 10 days; small windows were then made in the shells and the membranes were inoculated with the virus of São Paulo typhus (spleen of infected guineapigs). The virus was introduced by means of a sterile pipette between the membranes and the opening sealed with paraffin. The eggs were returned to the incubator for a further period of 3 to 5 days and examined by making sections of the membranes and staining by Gram and fuchsin. A portion of the thickened infested membrane was removed and injected into a guineapig; this animal developed fever but no Rickettsia could be found until the 3rd passage.

It is noteworthy that Rickettsia could not be found in the original inoculum (spleen of infected guineapig) but were found in section of the embryo membrane. D. H.

FRUGONI (C.). *Febbre bottonosa e sodoku.—Policlinico. Sez. Prat. 1935. Jan. 7. Vol. 42. No. 1. pp. 6-17. With 2 graphs & 1 fig.*

NICOLLE (Charles) & GIROUD (Paul). *L'observation des épidémies tunisiennes des typhus historique et murin et l'étude de leurs virus montrent que ces deux maladies sont étrangères l'une à l'autre.—C. R. Acad. Sci. 1934. Dec. 26. Vol. 199. No. 26. pp. 1553-1555.*

- DE OLIVEIRA CASTRO (G. M.) & BIER (Otto). Pesquisas sobre o tifo exantemático de São Paulo. Distribuição do virus no sangue.—*Rev. Med.-Cirurg. do Brasil*. 1935. Mar. Vol. 43. No. 3. pp. 97-101. With 1 fig.
- PANAYOTATOU (A.). Observations sur une communication de P. Lépine à propos du virus exanthématique d'Athènes.—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 833-834.
- SPÄT (W.). Fleckfieberstudien.—*Med. Klin.* 1934. Oct. 19. Vol. 30. No. 42. pp. 1395-1398.

CARRION'S DISEASE.

MACKEHENIE (Daniel). Verrue péruvienne et typhus exanthématiques. [**Verruga and Typhus.**].—*Rev. Sud-Américaine de Méd. et de Chirurg.* Paris. 1934. Dec. Vol. 5. No. 12. pp. 747-762. With 2 figs. [52 refs.]

The purpose of this paper is twofold :—

1. To supply to readers of the journal recent knowledge concerning Carrion's disease.
2. To repeat a suggestion made some ten years ago that Carrion's disease should be classed with the typhus-like diseases.

For 25 years, the author states, Peruvian medical men have recognized that Oroya fever and verruga peruviana are separate manifestations of one and the same disease.

He himself has seen several cases of severe fever with a pernicious type of anaemia which have recovered from that condition and have then developed a typical verruga rash with fever and muscular pains. CARRION inoculated himself from a verruga case, developed Oroya fever with extreme anaemia and died. ROSSELL on the other hand accidentally inoculated himself from a case of Oroya fever and developed verruga peruviana. Bartonella have been cultivated both from verruga eruption and from Oroya fever cases. These facts clearly prove that the conditions are merely symptoms of the same disease.

The name bacilliformis is unfortunate as the germ is not found in true homogeneous rods but the common form is a minute diplococcus, the two cocci being united by a clear capsule. In this form the organism is indistinguishable in the tissues or blood from Rickettsia. The methods which give the best results for the staining of Rickettsia are also best for Bartonella.

The method which the author has found best for demonstration of Rickettsia and Bartonella in the peripheral blood is to employ dehaemoglobinized thick films and to stain with ammoniated toluidine blue in methyl alcohol. Bartonella are found in the red cells whereas Rickettsia are not, and Bartonella can be cultivated in Novy-Nicolle blood agar whereas Rickettsia can only be cultivated in the presence of living tissue cells.

As regards the clinical aspect, apart from the anaemia and fever the author has noted a marked action of the germ on the central nervous system and this also links the disease with typhus, in fact in the early stages the two diseases are often confused.

The incubation period may last for some weeks and the course of the disease may be expressed somewhat graphically as follows :—

Incubation—latent period—anaemia—rash—latent period—immunity—the whole course lasting over many months; the germ has been cultivated from the blood over a period of one year.

After an experience lasting some 30 years the author considers that the severe fatal pernicious type of anaemia is now rarely met with and that the disease is altering in character just as other diseases have done in the course of time.

D. Harvey.

FROHN (W.). Ein Fall von Verruga peruviana (Carrionsche Krankheit). [**Case of Verruga Peruviana.**—*Dermat. Ztschr.* 1934. Feb. Vol. 68. No. 5. pp. 245–251. With 3 text figs.

A case of verruga observed in Europe and successfully treated with salvarsan.

A young man, a member of an expedition to South America, was severely bitten by sandflies while in the Peruvian Andes at an elevation of 17,000 feet. A few days later he developed fever and later became anaemic; he showed also symptoms of amoebic dysentery. He was invalided to Europe and on arrival in Hamburg one or two nodules were noted on the face and hands. In the clinic at Innsbruck the case was definitely diagnosed as verruga on the clinical picture and the histological findings on examination of the nodules; over 80 of these tumours were counted. Injections of salvarsan were quickly followed by disappearance of the rash.

D. H.

MALDONADO (Angel). Nuevo criterio para explicar la distribución geográfica de la enfermedad de Carrión.—*Crónica Méd.* Lima. 1933. Feb. Vol. 50. No. 836. pp. 41–48.

YELLOW FEVER.

MORGAN (M. T.). **Some Notes on a Tour of Inspection of the Co-operative Anti-Yellow Fever Service in Brazil.** With Appendix by J. A. KERR.—31 + 11 mimeographed pp. With 2 maps, 10 figs., 1 plan & 4 charts. [Report presented to the Office International d'Hygiène Publique, April-May Session, 1935, by the Delegate for Great Britain.]

An interesting account of the co-operative anti-yellow fever service in Brazil, together with general notes and observations obtained during the course of a visit to South America extending over a period of two months, during which the author was shown the details of the work being done by Dr. F. L. SOPER of the Rockefeller Foundation, and also spent nearly a month in the Planalto Region, where a rural type of yellow fever was in progress.

In a brief historical survey of yellow fever in Brazil attention is called to the marked changes that have resulted in our knowledge of the disease as a result of recent scientific discoveries. These may be summarized as follows :—

Previously.

Severe clinical disease considered typical ;

Absence of reported cases indicated absence of disease ;
Yellow fever essentially urban and transmitted only by *Aedes aegypti* ;

Key centre control believed effective in clearing surrounding area.

Now.

Severe classical case considered atypical in native population of endemic areas ;

Absence of reported cases not accepted as absence of disease ;
Yellow fever may continue at least for a period of months in rural areas, with transmission by *Aedes aegypti*, or even in the absence of this mosquito ;

Key centre control not effective in Brazil.

The co-operative system, founded in 1930, embraces yellow fever control throughout the whole of Brazil and is entirely Brazilian, staffed with Brazilian officers and men, but with the direction and advice of experts of the Rockefeller Foundation. It can be divided, arbitrarily, into five main divisions.

1. *The administrative service*, technically a division of the Federal public health service, with an annual cost of \$2,250,000 to which the Rockefeller Foundation contributes \$250,000.

2. *The anti-stegomyia service*, whose object is to clear towns of stegomyia, especially coastal towns, which may act as potential centres of infection. A number of teams have been appointed in each of the towns in which the service operates and details are given of the way in which they work. It has been found more economical to maintain a low index, less than 0.01 per cent., rather than to be satisfied with indices of 1 per cent. to 5 per cent. and a series of charts shows the results that have been obtained. Apart from its primary object the psychological effects of mosquito suppression are very beneficial, and at present the use of mosquito nets has disappeared from Rio de Janeiro and many other towns which formerly had the worst of reputations for yellow fever.

3. *Mouse-protection test surveys*, which are a valuable indication of where to suspect the disease and where to direct measures for control. The results of tests in the younger age groups in the Amazon Valley, where yellow fever has not been recognized during 20 years, indicate that a war in this district, with the consequent movement of non-immune troops, might well result in disastrous outbreaks of the disease, such as occurred at Santa Cruz, Bolivia, in 1932.

4. *Viscerotomy service*, whereby a routine collection of liver specimens is made at any centre, where either protection tests or doubtful clinical cases lead to any suspicion of the existence of yellow fever. [For details of the method of collection and the results of examination see this *Bulletin*, Vol. 31, p. 836.]

The organization of this service is based on the following assumptions :—

(a) That the existence of yellow fever in a community over a period of months will result in some fatal infections ; (b) that the yellow fever liver usually carries characteristic lesions ; and (c) that, when fatal yellow fever kills rapidly, its victims rarely surviving more than 10 days.

5. *Field surveys*, in hitherto uninvestigated areas, which are a constant feature of the Brazilian service. Reference is made to two of them which resulted in the discovery of a rural endemicity hitherto quite unsuspected. The first of these was the well-known discovery of yellow fever without *Aedes aegypti*, in the Valle do Chanaan, Espirito Santo [see this *Bulletin*, Vol. 31, p. 77] and the second, an outbreak first recognized in April, 1934, in the Planalto of Matto Grosso. The author had the opportunity of visiting this very remote part of the world which has never been properly surveyed and borders unexplored country. The area affected was part of this sparsely populated region on the plateau dividing the head waters of the Amazon and Paraguay rivers. Blood protection tests from 343 inhabitants of the region showed 67 positive, 274 negative and 2 doubtful. *Aedes aegypti* seems to be absent, but *Aedes scapularis* is abundant during the wet season and may be the carrier. Since the inhabitants live in isolated clearings in the forest it is improbable that man is the reservoir. The only animal in any numbers that moves from place to place is the monkey which abounds in the forest. The possibility of monkeys acting as reservoirs of infection is supported by the fact that three out of four specimens of blood from monkeys living in the vicinity of an Ecuador epidemic were found to protect mice.

These two epidemics in sparsely populated rural areas show that the old conceptions of yellow fever as essentially a disease of large towns must be abandoned. On the day of leaving Rio de Janeiro, the author was informed of the discovery of a positive liver specimen from the vicinity of Goyaz, and according to latest reports there is a widespread epidemic in that region, with more than 100 deaths up to date. Here again *Aedes aegypti* seems to be absent.

In conclusion the author pays a tribute to the work of the Federal Yellow Fever Service in Brazil.

The appendix by Dr. J. A. Kerr contains a useful account of the technique that has been adopted for dealing with the very large numbers of tissue specimens sent to the laboratory as a result of the viscerotomy regulations.

E. Hindle.

SUSSINI (Miguel), VACCAREZZA (Raul F.) & ALVARADO (Carlos Alberto). Profilaxis de la fiebre amarilla. Organizacion del servicio en el Norte Argentino. [**Organization of the Yellow Fever Preventive Service in Northern Argentine.**].—131 pp. With 9 maps & 21 figs. Publicado en Los Anales del Departamento Nacional de Higiene. 1934. Buenos Aires. P. Ventriglia.

An interesting and instructive account of the measures undertaken to deal with the menace of invasion of the Northern Argentine by yellow fever. Establishment of the Service was stimulated by the outbreak in Santa Cruz de la Sierra (Bolivia) in April 1932. Investigation of seven districts revealed that *Aedes* breeding was abundant in five. In July four sanitary stations were created, at Aguaray, Tartagal, Embarcación and Orán; later two more, at Ledesma and Formosa, with sanitary posts in five other districts.

The authors next give a geographical description of the zones threatened, followed by details of the measures adopted, the subjects being considered in the following order:—

1. The factors concerned: *Aedes aegypti* and its bionomics; the human susceptible host, telluric conditions, soil, humidity, temperature, etc.

2. The general plan of campaign: education of the people, personal protection, larvicides and the introduction of larvivoracious fish. A later chapter treats of these last in detail; the species utilized were *Aphyocharax erythrurus*, *Bryconamericus stramineus*, *Poecilurichthys bimaculatus* and *Aequidens vittatus* and descriptions and illustrations are given of all four.

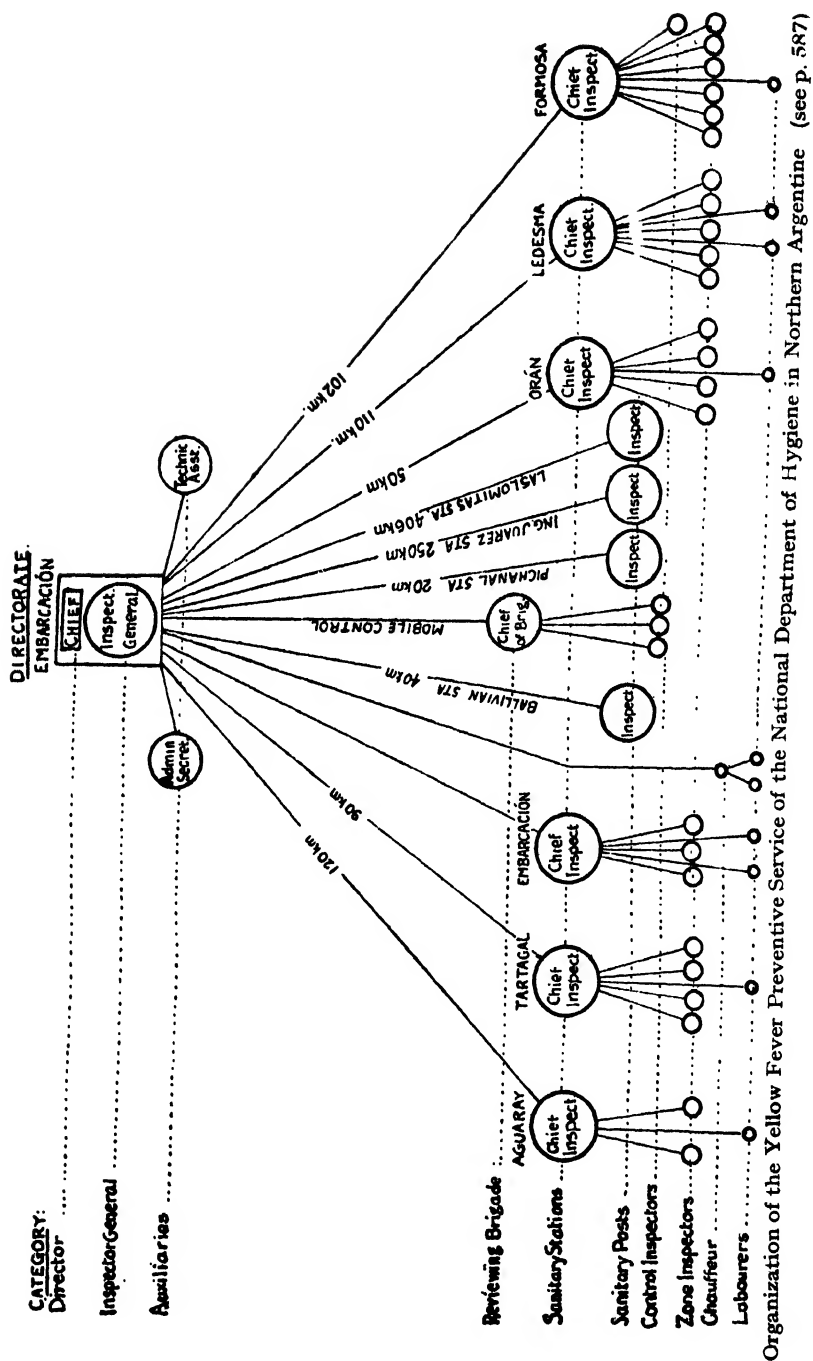
3. The forms to be filled in are referred to and in an appendix copies are given indicating the information required regarding patients, their surroundings and circumstances, water supply, etc., and the action taken to deal with the conditions found. In an appendix are printed the rules, regulations and instructions for the guidance of the various officials connected with the Service, and copies of the notices sent out and the forms to be filled in.

4. Next is a clear account of the personnel of management and control which is well seen in the accompanying scheme (p. 588).

The story is then related of the development of the campaign and the results achieved by it in the different areas selected for special and intensive measures. Illustrations are given to point out the prevailing defects, collections of rubbish and so forth [but these are poorly reproduced and far from distinct even in the original; they have no legend and are consequently not easy to interpret and in fact this can only be done by reference to the text].

Another chapter treats of the distribution and density of *Aedes aegypti* in Northern Argentine, where the index of the number of dwellings infected to the number inspected varied in the district of the campaign up to 90 per cent. in Ballivián and outside the zone of its action from nil in Cerrillos to 66.9 in Estación Perico. An accompanying map gives much information on this point but unfortunately is too indistinct in the original to bear reproduction.

H. H. S.



GOURVIL (E.). L'endémicité amaryle chez les indigènes du Soudan. [Yellow Fever Endemicity in the Natives of the (French) Sudan.]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 31-32.

The author gives notes on small outbreaks of yellow fever in Sikasso during 1931, and in Kayo, during 1931 and 1932, which support the view that the infection is widespread among natives of the French Sudan. Segregation of European habitations from the native quarters is advocated. E. H.

GOURVIL (E.). Remarques à l'occasion d'une épidémie de fièvre jaune. [Remarks on the Occurrence of a Yellow Fever Epidemic.]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 32-34.

A brief summary of the clinical symptoms observed in seven cases (five fatal) of yellow fever among Europeans at Sikasso in 1931. In every case except one the typically severe headache—"coup de barre"—was absent, and the patients merely felt extreme lassitude without any localized pains. Vomiting was a constant feature, although curiously enough the two cases showing "black vomit" were the only ones who recovered. Albuminuria was generally present but the urine of one of the patients, collected shortly before death, was negative. A slight degree of jaundice was the rule, but never very pronounced. All the patients showed extreme prostration, and during the apyretic phase some of them presented typical nervous symptoms, which always indicated a very grave prognosis. E. H.

PUBLIC HEALTH REPORTS. 1935. Jan. 25. Vol. 50. No. 4 pp. 101-102.—Yellow Fever and the Recent Decree on "Viscerotomy" in Colombia.

A discussion by Dr. G. BEVIER concerning the purpose of making viscerotomy compulsory, in certain cases, in order to clear up the situation with regard to rumours of yellow fever outbreaks in Colombia.

In addition to earlier outbreaks that have been subsequently diagnosed by means of the protection test many suspicious cases have occurred at Muzo. During 1934, in January, March and June, small outbreaks occurred there, and in the last two the diagnosis of yellow fever was confirmed by both pathological examination and protection tests. Several deaths suggestive of yellow fever also occurred in Caparrapi during 1933 and at the beginning of 1934. Judging from these results the disease seems to be gradually spreading westward and it is feared that it may reach Puerto Leivano, Guaduas, Utica, or Villeta. An epidemic with suspicious signs has developed in the vicinity of Restrepo (Meta) and is being investigated at present. It is evident that yellow fever is still a problem in Colombia and possibly a menace; the National Department of Health is therefore organizing a special unit to study the disease. E. H.

NICOLLE (Ch.). Au sujet de la vaccination contre la fièvre jaune. [Concerning Vaccination against Yellow Fever.]—*Bull. Acad. Méd.* 1935. Feb. 19. 99th Year. 3rd Ser. Vol. 113. No. 7. pp. 254-256.

The author discusses the advantages of vaccination by means of living and attenuated virus alone, compared with the use of virus and

immune serum. From a practical point of view it is concluded that sero-vaccination must now be replaced by the use of virus alone, since it has been shown to be innocuous, and to produce an active immunity.

E. H.

PUBLIC HEALTH REPORTS. 1935. Mar. 15. Vol. 50. No. 11. pp. 360-371. **Yellow Fever. Some Recent Contributions to our Knowledge of the Prevalence and Control of the Disease.**

A useful summary of recent publications, especially regarding the occurrence of yellow fever and methods of protection, printed for the information of quarantine officers and others interested in the subject.

E. H.

FINDLAY (G. M.) & CLARKE (L. P.). **Reconversion of the Neurotropic into the Viscerotropic Strain of Yellow Fever Virus in Rhesus Monkeys.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 6. pp. 579-600. With 2 text figs. & 8 figs. on 2 plates. [27 refs.]

An important paper showing that it is possible to reconvert neurotropic yellow fever virus into the ordinary viscerotropic type.

The virus used in these experiments had undergone 182 to 212 passages in the brains of mice and was a typical neurotropic strain. When inoculated directly into the livers of rhesus monkeys it gave rise to lesions in the liver, less extensive than but similar in type to those caused by ordinary viscerotropic virus. Further subcutaneous injections of virus obtained from intrahepatic passage resulted in the production in rhesus monkeys of typical yellow fever with lesions in the liver, stomach, kidney and heart. Intracerebral inoculations of this virus into monkeys gave rise to similar lesions associated with varying degrees of encephalitis.

This reconverted virus behaved as a typical viscerotropic virus not only in rhesus monkeys but also in white mice and hedgehogs. It again lost its viscerotropic pathogenicity after repeated intracerebral passages in mice.

In an interesting discussion of the constitution of yellow fever virus the authors come to the conclusion that the ordinary viscerotropic and fixed neurotropic strains represent two extreme types connected by a series of intergrades or intermediate types in which either viscerotropic or neurotropic pathogenicity may predominate, according to the animal species inoculated, the tissue in which the virus grows, and also individual idiosyncrasy.

The fact that in the laboratory the virus of yellow fever can be induced to undergo such rapid changes in its pathogenicity raises the question whether similar changes may not sometimes occur under natural conditions in the field.

E. H.

THEILER (Max) & HUGHES (Thomas P.). **Studies of Circulating Virus and Protective Antibodies in Susceptible and Relatively Insusceptible Monkeys after Inoculation with Yellow Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 481-500. With 10 charts. [20 refs.]

The authors have determined the virus content and development of protective antibodies in various species of *Macaca* and *Lasiopyga*

inoculated in various ways with either unmodified viscerotropic yellow fever virus or the modified neurotropic strain.

Their results show that when susceptible monkeys, including *Macaca mulatta* (= *Macacus rhesus*) and *M. cynomolga*, are inoculated by any route with unmodified yellow fever virus, extensive multiplication of the virus occurs, usually followed by death. In some instances there is multiplication of virus without any obvious signs of infection but followed by immunization. When very small doses were used (0.0000001 cc. serum virus) the incubation period might be prolonged to as much as 14 days, but as a rule the maximum quantity of virus in the serum was reached in about 3 days. Protective antibodies appear in the serum a few days after the virus can be detected in the blood stream; in fatal infections they may or may not be formed, but do not arrest the course of the disease.

The modified neurotropic virus, when inoculated by any route, also multiplies and gives rise to antibody formation. If this virus comes into contact with brain tissue, either by intracerebral inoculation or any other brain injury, encephalitis results.

The inoculation of both kinds of virus into African green monkeys, *Lasiopyga callitrichus*, was followed by multiplication, usually without symptoms, and by the subsequent development of protective antibodies. If the virus was inoculated intracerebrally, encephalitis resulted. Apart from the decreased response to unmodified virus, inoculated either intraperitoneally or subcutaneously, the reaction of these animals to yellow fever virus seems to be essentially the same as that of *rhesus* monkeys.

E. H.

SELLARDS (Andrew Watson). **The Infection and Immunization of Mice by Intraperitoneal and Subcutaneous Injection of the Virus of Yellow Fever.**—*Ann. Trop. Med. & Parasit.* 1935. Apr. 25. Vol. 29. No. 1. pp. 55–68. [15 refs.]

A study of the effects of extra-neural injections of yellow fever virus into mice, with special reference to immunity and to inapparent infection.

Mice that had been inoculated either subcutaneously or intraperitoneally with neurotropic or ordinary virus, were subsequently tested for inapparent infection mainly by three procedures:—(1) the intracerebral inoculation of their blood and other tissues into normal mice; (2) tests for active or passive immunity; (3) the intracerebral injection of sterile starch paste to facilitate the localization of virus in the brain.

Only a small proportion of the inoculated mice died of encephalitis, and of the survivors in some instances the virus died without producing any effect and in other cases an active immunity developed.

The intracerebral inoculation of blood and heavy suspensions of liver, spleen, adrenals and kidney, of mice that had been injected extraneurally with neurotropic virus, in no case resulted in the production of encephalitis.

The development of active immunity in mice which remained apparently well after the extraneural injection of neurotropic virus affords strong evidence of an inapparent infection, but there is some suggestion that after longer passages in the brains of mice, the virus becomes less effective in producing immunity. Mice that have survived an intracerebral inoculation of virus do not remain refractory,

but even after a few months may become infected by a second inoculation.

Two lots of 25 mice were inoculated, one lot subcutaneously and the other intraperitoneally, with viscerotropic virus. One of the first and two of the second lot died of encephalitis, and only seven out of the total survivors were immune against a subsequent intracerebral inoculation of virus.

A further batch of mice was inoculated either subcutaneously or intraperitoneally with neurotropic virus. These two groups were then divided into several lots of 6 each. On each successive day for 6 days one lot from each group was inoculated intracerebrally with starch. The results show that many of the intraperitoneal group (15 of 41) died of encephalitis, but only 6 survivors were immune; whilst in the subcutaneous group 6 out of 41 died of encephalitis, but 18 were immunized.

A second experiment gave similar results, which are interpreted as showing that there is less danger of invasion of the blood stream after subcutaneous than after intraperitoneal inoculation. *E. H.*

ADVIER. Etude expérimentale de la fièvre jaune. [**An Experimental Study of Yellow Fever.**]—*Ann. de Méd. et de Pharm. Colon.* 1934. Oct.—Nov.—Dec. Vol. 32. No. 4. pp. 441–472.

A detailed account of experiments confirming most of the well-known facts regarding the infection of monkeys and mice with yellow fever and the technique of protection tests.

A strain of yellow fever was obtained from a fatal case of the disease in a European. Although two monkeys were successfully infected with this strain and died with typical symptoms, the author failed to establish the strain in mice by intracerebral inoculation. It is noted that infected blood from this case of yellow fever had lost its infectivity when mixed with broth and kept at 37°C. for 24 hours, whilst a similar mixture kept in the ice chest remained infective. *E. H.*

SELLARDS (Andrew Watson). **The Interpretation of the Incubation Period of the Virus of Yellow Fever in the Mosquito (*Aedes aegypti*).**—*Ann. Trop. Med. & Parasit.* 1935. Apr. 25. Vol. 29. No. 1. pp. 49–53. [10 refs.]

An interesting discussion of the significance of the incubation period of yellow fever virus in the mosquito.

In opposition to the view of DAVIS, FROBISHER and LLOYD [see this *Bulletin*, Vol. 31, p. 81] who concluded that the incubation was required not for the multiplication of virus, but for its migration to the salivary glands, the author prefers the view that the virus multiplies in its insect host. The initial loss of the virus content in the mosquito is paralleled by many examples in protozoal infections, when after being ingested by a suitable host many of the parasites die, and only a few establish themselves and multiply. It is pointed out that under the same temperature conditions the incubation period of the virus is similar in both its vertebrate and invertebrate hosts (4 days at 37°C. in the mosquito). The lengthening of the incubation period as the temperature is lowered is consistent with the view that the virus grows more readily at a higher temperature, and the experiments

recorded by DAVIS and his associates are regarded as furnishing evidence that the virus multiplies in the insect host. *E. H.*

FINDLAY (G. M.) & STERN (Ruby O.). **Encephalomyelitis produced by Neurotropic Yellow Fever Virus.**—*Jl. Path. & Bact.* 1935. Mar. Vol. 40. No. 2. pp. 311–318. With 10 figs. on 3 plates. [18 refs.]

A record of the lesions produced in the central nervous system of susceptible animals—monkeys, guineapigs, mice and hedgehogs—after infection with neurotropic yellow fever virus.

In every case the virus produced an inflammatory reaction in the central nervous system, degenerative changes in the nerve cells, and acidophilic intranuclear inclusions. The inflammatory reaction was characterized by infiltration with mononuclear cells and proliferation of the microglia; it was much less marked in animals inoculated either subcutaneously or intranasally.

Degenerative changes in the ganglion cells were present in all stages from slight swelling of the cell body to neuronophagia with complete disintegration of the cell. The specific acidophilic intranuclear inclusions were seen only in ganglion cells which had not undergone extensive degeneration and never in cells showing neuronophagia. These inclusions did not stain with the Feulgen technique and were larger than the acidophilic granules sometimes found in the nerve cells of these animals, which are stained by this method. Demyelination was not observed. *E. H.*

BAUER (Johannes H.) & HUGHES (Thomas P.). **Ultrafiltration Studies with Yellow Fever Virus.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 101–110. [14 refs.]

A record of filtration experiments with two strains of yellow fever virus, confirming FINDLAY and BROOM's estimate of the size of the virus particles, and their observation that in this respect there is no difference between neurotropic and viscerotropic strains. [See this *Bulletin*, Vol. 31, p. 499.] *E. H.*

SHANNON (Raymond C.) ; PUTNAM (Persis). **The Biology of *Stegomyia* under Laboratory Conditions. I. The Analysis of Factors which Influence Larval Development** [SHANNON & PUTNAM]. **II. Egg-Laying Capacity and Longevity of Adults** [PUTNAM & SHANNON].—Reprinted from *Proc. Entom. Soc. Washington*. 1934. Oct. Vol. 36. No. 7. pp. 185–216. With 9 figs. [15 refs.]; pp. 217–242. With 5 figs.

The authors desire to put our knowledge of the biology of the yellow-fever mosquito on a solid quantitative basis. In the present papers they set out a considerable body of numerical fact.

The papers contain a mass of useful work, carefully recorded. Among other things they tell us the conditions under which the maximum number of mature dry eggs will hatch quickly. The authors find considerable differences between their results and those published by other workers, and the view is expressed that these may be due to differences in the strain of *Stegomyia*; is it not equally possible that

they are due to different conditions or to the presence of micro-organisms in the water? The matter could perhaps best be investigated if experiments with different strains were carried out side by side under aseptic conditions. With regard to the biology of the larva, facts are given about the mortality under certain standard laboratory conditions. One observes that with improved technique the mortality was lowered, and also that a greater uniformity in rate of development followed. Studies were also made on the mortality caused by overcrowding. Reference is made to the optimum conditions, but they are in no way defined.

Biological studies on the adult female give information on the number of eggs which are laid under certain conditions of feeding, etc. Here comparison is also made between the mortality of females which were given blood at regular intervals (and which therefore laid eggs) and others which never received blood and which were kept alive with honey and water. In the second group there were very few deaths in the first ten weeks, after which the number of deaths suddenly became great. The curve relating mortality to time therefore approaches the rectangular; but the corresponding curve for the females which received blood and laid eggs is of the more usual S shape.

In certain parts of the paper it seems that the statistical analysis has been carried further than the accuracy of the experiments warrants; for instance, the authors give facts on the mean duration of larval life as affected by temperature, but temperature was not controlled and was measured in the air of the laboratory, not in the breeding jars, at 8 a.m. and 4.30 p.m. There is therefore no evidence that the mean temperatures recorded were close to the mean temperatures to which the insects were exposed; but in spite of this comparative crudity in the experiments, the statistical analysis is of a high degree of elaboration.

P. A. Buxton.

ROZEBOOM (Lloyd E.). **The Relation of Bacteria and Bacterial Filtrates to the Development of Mosquito Larvae.**—*Amer. J. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 167-179.

The author has set himself to discover whether mosquito larvae (generally those of *Aedes aegypti*) can breed in sterile water containing organic material in solution, and whether the larvae grow as well in a pure culture of known bacteria as they do in unsterilized water containing bread crumbs.

The eggs were sterilized in hexylresorcinol, and controls transferred to a suitable unsterile medium hatched well. The sterility of the experimental tubes was examined by testing for aerobes and anaerobes. Since the rate of growth of larvae is used as a criterion, it would have been well to control the temperature. The paper describes a large number of experiments in which the results appear clear and consistent. The most important findings are that larvae in sterile filtered water taken from breeding places lived no longer than those in sterile distilled water, none of them reaching the second stage. Larvae provided with living pure cultures of known micro-organisms were able to grow, though not always as rapidly as the controls: adults were generally produced, though the larval mortality was high in most cases. The author provides support for his view that it is the bacteria and not the results of their metabolism on which the larvae live.

The interesting observation was made that larvae live long but grow very slowly in an autoclaved mixture of water and bread crumbs. It would be interesting and valuable to test the result of adding salts, possibly nutritive materials, accessory food factors, etc., and the author has begun to explore this subject.

P. A. Buxton.

HOFFMANN (W. H.). Tropenarzt und Gelbfieber.—Reprinted from *Jahrbuch d. Miss. ärztl. Inst. z. Würzburg*. 1934. Vol. 11. p. 19.

SOPER (Fred L.). El problema de la fiebre amarilla en América.—*Bol. Oficina Sanitaria Panamericana*. 1935. Mar. Vol. 14. No. 3. pp. 204–213.

RELAPSING FEVER AND OTHER SPIROCHAETOSSES.

SINGER (Ernst). Die Wirkungsweise der Chemotherapeutika bei Spirochäten- und Protozoeninfektionen. [**The Mode of Action of Chemotherapeutic Substances in Spirochaetal and Protozoal Infections.**—*Med. Klin.* 1935. Mar. 22. Vol. 31. No. 12 (1579). pp. 386-389.

A useful summary of the author's view on the mode of action of chemotherapeutic agents, based mainly on the results obtained by the analysis of spirochaetes and trypanosomes before and after treatment with various arsenical and gold preparations [see this *Bulletin*, Vol. 31, p. 510].

He emphasizes that the direct action of chemotherapeutic agents on spirochaetes and trypanosomes, as shown by the rapid disappearance of these organisms from the blood, is only one part of the curative action. The other part depends on the immune reaction of the host, especially the influence of the chemotherapeutic agent on the cells of the host, but this is a pharmacological problem about which relatively little is known at present. However, the methods of analysis which have been developed for the examination of spirochaetes and trypanosomes are applicable to the study of what happens to chemotherapeutic agents in the tissues of the host, and seem likely to lead to fruitful results.

E. Hindle.

VON JANCsó (N.) & NOVÁK (E.). Mikrobiologische Grundlagen der chemotherapeutischen Wirkung. II. Mitteilung: Mikroskopischer Nachweis des chemotherapeutisch verabreichten Goldes in Spirochäten, Trypanosomen und Bakterien durch Ultrakristallisation. [**A Microbiological Basis for Chemotherapeutic Action. Part II. The Microscopic Demonstration of Chemotherapeutic Gold in Spirochaetes, Trypanosomes and Bacteria by Means of Ultra-Crystallization.**—*Zent. f. Bakt.* I. Abt. Orig. 1935. Apr. 25. Vol. 134. No. 1/2. pp. 76-86. With 2 text figs. [15 refs.]

The authors have used the fact that extremely small quantities of gold can be seen by means of dark ground illumination to demonstrate its presence in spirochaetes from infected rats and mice treated with various gold compounds.

The animals were infected with a Russian strain of *S. recurrentis* and at the height of the infection injected with potassium gold cyanide, Solganal A or B, or similar compounds. One hour after treatment the spirochaetes show a massive impregnation with gold and in thin air-dried films examined by means of dark ground illumination the parasites stand out in bright gold on a black background.

For the preparation of films three methods are recommended :—

(1) Extremely thin smears of defibrinated blood containing the spirochaetes after treatment.

(2) The incineration method, applied to concentrated masses of spirochaetes obtained by centrifugation. The heart blood of an infected rat after treatment is defibrinated, then centrifuged at about 1,000 revolutions per minute to remove any blood cells. The supernatant fluid is spun at about 7,500 revolutions per minute to bring down the spirochaetes,

which are then washed twice in either human serum or filtered sheep serum. Smears are made of the concentrated spirochaetes on slides which will withstand heat and on which there is no trace of any fat or minute scratches. The slides are then heated above a Bunsen flame, at first film side upwards until the film turns brown, and finally with the film side downwards until the slide is red hot. The slides are allowed to cool slowly and when examined by dark ground illumination the spirochaetes, represented only by ash containing gold particles, stand out against the dark background.

(3) Permanent preparations can be made by placing air-dried films in a developing solution which must be freshly prepared and is composed of:—

- 100 cc. Distilled water.
- 2.5 cc. Gold chloride solution.
- 3.0 cc. Potassium carbonate solution.
- 1.25 cc. Potassium ferricyanide solution.

The gold chloride solution contains 2.51 gm. Au Cl_3 (= 3.49 gm. of crystallized $\text{Au Cl}_3 \cdot 4 \text{H}_2\text{O}$) per litre. The potassium carbonate 12.4 gm. K_2CO_3 per litre, and the potassium ferricyanide 0.11 gm. $\text{K}_3\text{Fe}(\text{CN})_6$ per litre. In every case double distilled water is used.

The films are immersed in this developing solution and heated to 90°C . ; then 4.0 cc. of 1 per cent. fresh formalin solution is added and the mixture kept warm for about three minutes and then the slides washed in distilled water and allowed to dry. The formalin solution consists of 1 cc. acid-free formalin and 99 cc. of distilled water.

Finally the films may be mounted in neutral Canada balsam and examined by means of dark ground illumination.

These methods may be used not only to demonstrate whether any particular gold compound unites with the spirochaetes, but also to study relative localization of gold in the tissues of treated animals, for control preparations made from material not containing gold did not show the characteristic appearance under the dark ground. The authors recommend its use for the study of trypanosomes, tubercle bacilli and similar infections where gold compounds may be of value.

E. H.

ROSENHOLZ (H. P.) & SCHERBINA (L. I.). Zur Frage der sogenannten "Pseudoinfektion" bei Rückfallfieber und ihre chemotherapeutische Behandlung. [The Problem of So-called "Pseudoinfection" in Relapsing Fever and its Chemotherapeutic Treatment.]—*Zent. f. Bakt.* I. Abt. Orig. 1935. Apr. 25. Vol. 134. No. 1/2. pp. 42-50.

The injection of mice with blood containing a Russian strain of *S. recurrentis* is said to be followed by a pseudoinfection.

This is characterized by (1) the absence of any incubation period, spirochaetes appearing in the circulation within one or two hours after inoculation ; (2) by the type of increase and decrease in the number of spirochaetes in the peripheral circulation ; (3) by the absence of any immunity against reinfection ; (4) by the absence of any specific antibodies after the disappearance of the spirochaetes ; (5) by the failure to produce any passive immunity with the blood of recovered mice ; and (6) by the failure of salvarsan to have any sterilizing action on these infections.

The latter observation supports the view that the action of salvarsan and similar compounds is linked up with the natural defence mechanism of the host, and consequently when this is not brought into action, as in the case of these pseudo-infections, the drug has no effect on the parasites. E. H.

SCHOLER (Hans). Isolierung einer Pseudospirochäte aus dem strömenden Blut bei einer rückfallfieberartigen Erkrankung. [**The Isolation of a Pseudo-Spirochaete from the Circulating Blood of a Patient showing a Type of Relapsing Fever.**—*Klin. Woch.* 1935. Mar. 9. Vol. 14. No. 10. pp. 333–338. With 1 fig. [22 refs.]

A detailed account of a patient in Basle, who during a period of about 6 weeks suffered from a peculiar type of relapsing fever of obscure aetiology.

Blood cultures were made in Schiödt's medium and on two occasions the author obtained strains of a pleomorphic organism ranging in form from short vibrios $2\ \mu$ in length up to spiral forms $30\ \mu$ in length, but thicker than ordinary relapsing fever spirochaetes. The inoculation of these cultures into mice, pigeons and guineapigs gave negative results, but when inoculated into the eye of a rabbit a "primary effect" in the form of keratitis and iritis was noticed after 2 to 3 days.

The patient was given injections of "syntharsan" starting on the 27th day of illness; blood cultures made three weeks after this treatment had begun were negative and the patient's symptoms gradually disappeared.

The nature of the organism isolated by the author remains doubtful, but is considered as possibly related to spirochaetes in view of its characters and also the susceptibility of the infection to treatment with neosalvarsan. E. H.

KNOWLES (R.) & BASU (B. C.). **A Blood-Inhabiting Spirochaete of the Guinea-Pig.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 449–468. With 2 charts, 3 text figs. & 4 figs. on 1 plate. [19 refs.]

The description of a spirochaete, named by the authors *Spirochaeta cobayae*, found occurring naturally in the blood of a guineapig at Muktesar.

The infection was easily transmitted from one guineapig to another and also to white rats and rabbits by means of blood inoculation. After an incubation period of 2 to 6 days spirochaetes appeared in the blood, were present from 7 to 28 days and then disappeared. The mortality was about 31 per cent., animals dying either at the height of infection or a few days after the spirochaetes had disappeared. Relapses occurred in 9 out of 69 animals. The infection was not hereditarily transmitted, and there was no transmitted immunity. Recovered animals showed a solid immunity.

The spirochaete belongs morphologically to the relapsing fever group and can be readily cultivated in Galloway's medium.

In *Argas persicus* the spirochaete is said to develop in a manner similar to *S. anserina* [see this *Bulletin*, Vol. 29, p. 592], and the

small spirochaetes invade the salivary glands. Although the authors failed to infect guineapigs by the bites of these ticks, the inoculation of emulsions of the salivary glands of the ticks was found to produce infection.
E. H.

BRUMPT (E.). Présentation de deux *Ornithodoros canestrinii* Bir., 1895, vivants originaires d'Ispahan (Perse). [**Presentation of Two Living *O. canestrinii* from Isfahan, Persia.**—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 51–53.]

O. canestrinii was described in 1895 by BIRULA from specimens collected at Teheran in 1839 and in the Caucasus in 1885. Brumpt had ticks collected in Persia and sent to Paris; two females (alive) and one male (dead) proved to be this large *Ornithodoros*. The females have fed but have not yet laid eggs. Brumpt intends making a study of them and seeing if they transmit *Spirochaeta persica*, the agent of the relapsing fever of Central Asia. He thinks the species must be rare, for it has not been found by the Russian zoologists who have studied the tick fauna of Turkestan.
A. G. B.

WYNNS (Harlin L.) & BECK (M. Dorothy). Epidemiological Studies on Relapsing Fever in California.—*Amer. Jl. Public Health.* 1935. Mar. Vol. 25. No. 3. pp. 270–276. With 2 maps. [13 refs.]

ZIMMERLI (E.). Is there any Bronchial Spirochaetosis?—*Jl. Egyptian Med. Assoc.* 1935. Jan. Vol. 18. No. 1. pp. 32–38. [See this *Bulletin*, Vol. 31, p. 850.]

RAT-BITE FEVER.

PANDALAI (N. G.). **Observations on the Pathogenicity of the Local Strains of *Spirillum minus* to Guinea-Pigs.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 469–473.

Rat-bite fever seems to be not uncommon in Vizagapatam, since about a dozen cases a year go to the laboratory for diagnosis. The author gives details of four cases from which strains of *S. minus* were isolated and studied in regard to their pathogenicity to guineapigs and immunological reactions.

Two of the strains produced fatal infections in guineapigs, another strain a non-fatal infection, whilst the fourth was non-pathogenic. Sub-passages tended to exalt the virulence of the parasite.

Positive Wassermann reactions in many of the infected guineapigs showed that a complement-fixing antibody, identical with the syphilitic reagin in its physico-chemical properties, is produced by infection with *S. minus*. The experimental disease in guineapigs was easily cured by injections of novarsenobillon.
E. Hindle.

GAUTIER (Claude) & BISSERY. Un cas de sodoku. [**A Case of Sodoku.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935. Mar. 11. 51st Year. 3rd Ser. No. 8. pp. 358–363. With 1 chart.

The description of a typical case of sodoku in France in which the infection was acquired in a peculiar manner. Whilst feeding a falcon with a freshly killed rat, the beak of the bird scratched the patient's forefinger, which was covered with the blood of the rat, and after an incubation period of 4 to 5 days he developed a typical attack of the disease, which was cured by intravenous injections of neosalvarsan.

E. H.

GIRARD & PAULICEVICH. Deux cas de sodoku dans la région toulonnaise. [**Two Cases of Sodoku in the Neighbourhood of Toulon.**]—*Marseille-Méd.* 1935. Feb. 5. Vol. 72. No. 4. pp. 156–164. With 4 charts.

A description of two typical cases of sodoku in children, both of whom had been bitten by rats. *S. minus* was found microscopically in the blood, but attempts to infect guineapigs were negative. Both cases responded to treatment with arsenical compounds. E. H.

FRANCO (J. Jiménez) & COLICHÓN (Héctor). Periorquitis y edema escrotal consecutivos a la inoculación experimental de *Spirilla minus*. [**Periorchitis and Scrotal Oedema after Inoculation with Spirillum minus.**]—*Rev. Méd. Peruana.* 1934. Dec. Vol. 6. No. 72. pp. 2180–2186. With 3 figs.

After inoculation of guineapigs with the blood or emulsions of the organs of an animal suffering from rat-bite fever the scrotal or scrototesticular reaction is set up, as in typhus, and is with difficulty, if at all, distinguishable from it. Other considerations have to be taken into account. Thus in experimental murine typhus recovery is the rule, most cases of sodoku end fatally; other symptoms—adenitis, blepharitis, emaciation—may assist; the route of inoculation is important, the reaction occurring after subperitoneal injection in the case of typhus, but after subcutaneous inoculation in sodoku. Lastly, the viruses are not mutually protective, an animal after it has been treated by novarsenobillon for its scrotal reaction due to rat-bite virus is still liable to give the reaction again when inoculated with the murine typhus virus. [See also this *Bulletin*, Vol. 30, p. 877.]

H. H. S.

LEPTOSPIROSIS.

UHLNTHUTH (P.) & ZIMMERMANN (E.). Beiträge zur Chemo- und Serotherapie der Weilschen Krankheit. [**A Study of the Chemo- and Sero-Therapy of Weil's Disease.**]—*Med. Klin.* 1935. Mar. 22. Vol. 31. No. 12 (1579). pp. 375–377. [14 refs.]

The authors give a brief summary of the results obtained in the treatment of Weil's disease by various bismuth compounds and also by means of immune serum. Their recent experiments show that

three new compounds, "R 141" (Rothmann), also "Bi 5" and especially "Bi 7" (Giemsa) are efficient agents for the treatment of guineapigs infected with Weil's disease, as indicated in the following table showing the results obtained with seven different preparations :—

	Minimum Lethal Dose		Minimum Curative Dose		Therapeutic Index
	Mg. of Compound	Mg. Bi	Mg. of Compound	Mg. Bi	
Bismuth-Yatren A (1% Bi)	0.5-0.6 ccm. solution	6	0.10-0.15 ccm. solution	1.5	1:5 (-1:8)
R 141 (40% Bi)	30-45	16	5-10	3	1:3-1:8
R 1220 (22.5% Bi)	200-250	48	about 40-60	11	1:3-1:5
Natrol (12.5% Bi)	40	5	15-20	2.3	1:2-1:3
Bi 5 (71% Bi)	about 50	36	6-8	5	1:7
Bi 7 (64% Bi)	about 80-100	58	about 8	5	1:10-1:12

In each case the dose is calculated per 100 gm. weight, and the guineapigs were inoculated subcutaneously with the therapeutic agent 24 hours after having received an intraperitoneal injection of the disease agent. "R 141" is a sodium compound of bismuth-dithiopyridine-carbonate; "Bi 5" (Pallicid) is sodium tribismuthyl tartrate; and "Bi 7," sodium dibismuthyl tartrate. The latter has the most favourable chemotherapeutic index of any compound tried, but as in the case of "Bi 5" it is advisable to inoculate it intramuscularly, or preferably intravenously, in order to avoid the local necrosis which may follow subcutaneous injections.

The action of immune serum is well known but the authors add some notes on its use in the treatment of human cases of Weil's disease. The serum should have an agglutination and lysis titre of at least 1:20,000. Human convalescent serum reaches its highest titre 30 to 50 days after the beginning of the attack. It deteriorates when stored and after 6 months should not be used. Rabbit immune serum gives good results and is now supplied by the I. G. Farbenindustrie (Behring Works, Marburg). The dose is 30-40 cc. of serum injected intramuscularly.

E. Hindle.

ZIMMERMANN (E.) & ARJONA (E.). Serologischer Titer und Heilwert der Seren gegen Weilsche Krankheit. [The Serological Titre and Therapeutic Action of Sera against Weil's Disease.]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Dec. 31. Vol. 84. No. 1. pp. 111-117.

The authors tested the agglutination titre of various human and rabbit anti-sera and then tested their action in guineapigs inoculated

with the sera respectively 4 or 5 days after being infected with *S. icterohaemorrhagiae*. The results show that the agglutination titre may range from 1 : 160,000 to 1 : 5,000 and is a clear indication of the value of the serum for treatment, but when convalescent serum is going to be used for the treatment of human cases its agglutination titre should not be less than 1 : 20,000. E. H.

TROISIER (J.), BARIÉTY (M.) & BROUET (G.). Spirochétose ictéro-hémorragique après morsure de rat. Méningite purulente. [**Spirochaetal Jaundice after the Bite of a Rat. Purulent Meningitis.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris*. 1934. Nov. 19. 3rd Ser. Vol. 50. No. 29. pp. 1451–1458.

A detailed description of a fatal case of this disease in a patient who was bitten by a wild rat and developed jaundice 15 to 20 days later. After entering hospital suppuration of the sub-arachnoidal spaces also developed, in addition to the usual symptoms of spirochaetal jaundice. E. H.

BARROS (Enrique). Espiroquetosis icterohemorrágica.—Reprinted from *Prensa Méd. Argentina*. 1935. Jan. 2, 9 & 16. 84 pp. With 4 figs. [174 refs.]

REVIEWS AND NOTICES.

BRITISH EMPIRE LEPROSY RELIEF ASSOCIATION. **Dawn ; being the Annual Report for 1934.**—36 pp. With 11 figs. 1935. London: 131 Baker Street, W.1.

The British Empire Leprosy Relief Association issues its Annual Report for 1934 under the title "Dawn," suggestive of the more hopeful outlook that the activities of the Association have brought to a class of people suffering from a disease formerly regarded as incurable. In the words of the report "the leper is slowly beginning to feel that he is not a doomed man . . . and that his return to a life of usefulness is not an impossibility."

The year 1934 marks the close of the first decade's work of the association. During these ten years over £18,000 has been given to medical missionaries and others for the erection of dispensaries, hospital buildings and houses for lepers, and more than £5,000, representing several million doses, has been spent in supplying a better and more effective derivative of chaulmoogra oil to those in a position adequately to treat cases. The grants have covered territories as far apart as the Solomon Islands in the Western Pacific, Burma, West Africa, East Africa, Rhodesia and the West Indies.

In India an appeal for funds issued by the Viceroy (Lord READING) brought in a sum of over £160,000 with the result that energetic and sustained action is being taken throughout that great country in the way of research, surveys and the treatment of those suffering from leprosy.

An interesting development of the Association's work has been the foundation of a Special Committee in conjunction with Toc H* to select and train non-medical men recommended by Toc H for employment in leper home colonies, leprosy prevention units, and such like schemes. So far this Special Committee has selected six of the most suitable men from a very long list of candidates. Five of these are now undergoing a nine months' elementary medical training at Livingstone College, Leyton, prior to being sent to Nigeria. The sixth man selected is being sent to the Leprosy Home and Hospital at Dichpali, H.E.H. The Nizam's Dominions, India.

Other activities of the Association referred to in the report are its publications and propaganda, and a tour of the West Indies in 1934 by its Medical Secretary.

The report shows that though much has been achieved by the Association during the first ten years, much more could be accomplished if the funds at its disposal were commensurate with its needs. R. L. S.

FRÓES (Heitor P.). *Lições de clinica tropical.* Vol. II. Livro I (2a Serie). *Estrongiloidíase. Filariases. Sodóco. Boubá. Micetoma podal. Dermatite linear serpiginosa.* [Lectures in Tropical Medicine.]—pp. vii + 311. With 126 figs. & 2 charts. 1934. Bahia.

The first volume of this work, of which apparently there are to be five when the whole is completed, dealt with malaria. That was issued in 1933. The present treats of infestations by *Strongyloides* (3 lectures), *Filaria* (2), with Rat-bite Fever, Yaws (2), *Mycetoma pedis* (2), and Creeping eruptions (2). The text has been carefully prepared, due acknowledgment is made to research workers in countries other than that of the author, references are abundant and

* 'Toc H' is an organization for social service, founded as a memorial to British youth who perished in the World War.

the information is full, up-to-date and clearly set out. There is little therefore to say except that to those who are conversant with Portuguese the whole will constitute an excellent text-book if the publication of the next three volumes can be expedited ; otherwise by the time the last is issued the first will be out-of-date. Where the text is so good it is a pity that, with certain exceptions, the illustrations are so poorly reproduced. Some we can follow after reading the legend, but some, *e.g.*, Figs. 18, 56 and 84 on pp. 63, 178 and 236 respectively, convey nothing to the reviewer even with the aid of the legend subscribed, and presumably the average reader will find similar difficulty in their interpretation.

H. H. S.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 9.]

RABIES.

A REVIEW OF RECENT ARTICLES, XXIII.*

i. *Virus.*

It will be remembered that NICOLAU and KOPCOWSKA¹ claimed that fixed virus could be retransformed into street virus by passage inoculations into the right sciatic nerve of emulsions obtained from the left sciatic nerve of the previous animal (this *Bulletin*, Vol. 31, p. 637). They have repeated this experiment using the ordinary Pasteur strain of fixed virus with the same result—namely a progressive increase in the number and size of the Negri bodies. KOPCOWSKA² in an additional paper states that the phenomenon of “septinévrite” is also gradually increased. Thus with the retransformed virus emulsions of the nerve trunks were found to be constantly infective—25 out of 25—whereas with fixed virus the proportion was 10 out of 13. This is considered to be additional evidence that the virus has been retransformed.

MANOUÉLIAN³ restates his view that the virulence of the saliva in rabies depends upon the presence of virus in the neurones of the salivary glands, and of the mucosa of the tongue. These neurones lie close to the surface, and a slight abrasion may set them free.

REMLINGER and BAILLY⁴ find that the Tangier strain of fixed virus has become less resistant to drying during the course of passaging. In 1923 when the virus was in its 2200th passage, cords dried for 6 and 5 days were never virulent, whereas of 15 cords dried for 4 days 7 were virulent. The experiment has been repeated in 1934, when the virus was in its 2670th passage. At this date 4-day dried cords were never virulent (0 in 12) whilst of 30 cords dried for 3 days 10 were virulent. Similarly, resistance to the action of glycerine has been reduced.

* For the twenty-second of this series see Vol. 32, p. 173.

¹ NICOLAU (S.) & KOPCOWSKA (L.). Sur la transformation du virus rabique fixe en virus des rues.—*C. R. Soc. Biol.* 1935. Vol. 119. No. 17. pp. 140–143. With 1 fig.

² KOPCOWSKA (L.). Septinévrite à virus rabique fixe “ramené en arrière” (transformé apparemment en virus des rues).—*C. R. Soc. Biol.* 1935. Vol. 119. No. 17. pp. 143–146. With 1 fig. [10 refs.]

³ MANOUÉLIAN (Yervante). Neurones virulents et infection de la salive au cours de la rage.—*C. R. Soc. Biol.* 1935. Vol. 119. No. 18. pp. 256–257.

⁴ REMLINGER (P.) & BAILLY (J.). Influence des passages de lapin à lapin sur la sensibilité du virus rabique à la dessiccation et à la glycérine.—*C. R. Soc. Biol.* 1935. Vol. 118. No. 12. pp. 1206–1208.

The effects of subpassage on the resistance of the virus to ether and to dilution are described in a second communication.⁵ It is shown that the resistance to ether increases as a function of the number of passages. In 1919 brain substance immersed in ether remained virulent for about 70 hours, now it is still virulent after 215 hours immersion. A similar increase is found to apply to dilution. REMLINGER and BAILLY believe that the confliction between these two results is more apparent than real. The effect of passage is to adapt the virus to the nervous substrate. Thus with passage the concentration of the virus, and in particular the concentration of young forms especially sensible to physical agencies such as desiccation, increases. Thus the effect of desiccation will increase with passage. Glycerine is not an antiseptic, but more a physical agency acting in virtue of its hygroscopic effects. Its action consequently increases with sub-passage, as the concentration of young forms becomes greater. Dilution on the other hand acts not by attenuation but by repartition, and ether—being an antiseptic—acts proportionately to the concentration of the virus. As the effect of subpassage is to increase the concentration of the virus, it takes an increasing period of time for complete disinfection to be achieved.

ANDO⁶ from a lengthy series of experiments finds that the incubation periods of different strains of fixed virus vary considerably. The infectivity to subcutaneous and intraplantar injection also varies. Some viruses are relatively weak when inoculated subcutaneously but show a high degree of virulence when introduced intracerebrally. There is also variability as regards the occurrence and types of the Negri bodies which are found in the inoculated animal (dog, rabbit or guineapig), some strains producing the larger forms seen in street virus infection. The fixed virus strains could not be serologically differentiated by means of rabicidal sera.

An interesting series of graphs showing the rise and fall of rabicidal power of the serum after immunization is given in the second section of this paper. For example the dilution of serum which inactivated "a definite quantity" of an emulsion of virus filtered through a Berkefeld V, and kept in contact *in vitro* for 2 hours at 37°C. was in one instance 1/4 on the 15th day, 1/16 on the 20th day, 1/64 on the 30th day, 1/128 on the 45th day, 1/32 on the 65th day, and 1/16 on the 90th day. With strains of short incubation the serum showed rabicidal properties earlier than with strains of long incubation, and fixed virus vaccine which had undergone few subpassages acted earlier than did vaccines which had undergone many subpassages.

In the third section ANDO discusses the question of the selection of a suitable strain of fixed virus for treatment. He considers that the strain must be "freshly fixed" and have a short incubation period. Its power of producing rabicidal substances as well as its power of protection should be tested. Its virulence should be tested by subcutaneous, intraplantar and intracerebral inoculation. Its peculiarities as regards Negri body production should also be investigated.

⁵ REMLINGER (P.) & BAILLY (J.). Influence des passages de lapin à lapin sur la sensibilité du virus rabique à l'éther et à la dilution.—*C. R. Soc. Biol.* 1935. Vol. 119. No. 16. pp. 29-31.

⁶ ANDO (Keizaburo). Untersuchungen ueber Virus-fixe der Lyssa. I. Virulenz des Virus-fixe und seine Klassifikation.—*Japanese Jl. Experim. Med.* 1935. Apr. 20. Vol. 13. No. 2. pp. 125-147. II. Vergleichende Immunisierungsversuche mit Virus-fixe Stämmen.—*Ibid.* pp. 149-157. With 9 figs. III. Ueber Virus-fixe-Stämme und ihre Auswahl.—*Ibid.* pp. 159-165. [78 refs.]

It will be remembered (this *Bulletin*, Vol. 31, p. 638) that SHORTT and BROOKS found that 10 minutes exposure of suspensions of fixed virus brain tissue to the photo-dynamic action of solutions of methylene blue completely inactivated the virus, whereas according to GALLOWAY's experiments the virus was inactivated in collodion membranes, or sand and paper-pulp filtrates, but not in unfiltered suspensions. GALLOWAY also found that after exposure the virus retained its antigenic value. The former authors⁷ have been unable to confirm this latter result. They find from experiments on 114 rabbits that the antigenic value is greatly impaired. They suggest that "if the photo-dynamic action of methylene blue is to be of any use in the preparation of vaccines its action must stop short of complete inactivation in the sense of a dead virus." As a source of light SHORTT and BROOKS used sunlight, and GALLOWAY a 300 candle power filament lamp. SANKARAN and BEER⁸ have now carried out a series of experiments in which a Quartz Mercury Vapour lamp was the source of radiation. They find that exposure of a 5 per cent. suspension of rabies infected brain to this radiation inactivates the virus in 10 minutes, and that this occurs even in the absence of methylene blue. Further experiments are being carried out to determine the physical basis of this phenomenon, and experiments are also in progress to determine whether the inactivated virus has retained its antigenic properties.

A similar result has been obtained by LEVADITI.⁹ The virus *in vitro* was destroyed in 5 minutes. Further experiments were carried out *in vivo*. It appeared that a single application of the lamp for 10 minutes to the cornea (after corneal inoculation) did not prevent infection in the case of 7 out of 9 rabbits irradiated immediately, 4, 24 and 48 hours and 3 days after inoculation. Three applications, each of 10 minutes duration, saved 4 out of 6 rabbits. The animals which survived from the former experiments were not immune to further infection. The author draws attention to the fact that the passage of the virus from the site of inoculation (neuroprobasie) must be extremely rapid.

In an article by LIMA¹⁰ are recapitulated the results of his experiments upon the transmission of the rabies of Matto Grosso by the vampire bat (this *Bulletin*, Vol. 31, p. 637).

REMLINGER and BAILLY¹¹ in continuance of their article (this *Bulletin*, Vol. 31, p. 639) present further results of their investigation of the pseudo rabies of AUJESZKY. The virus is sometimes found in the

⁷ SHORTT (H. E.) & BROOKS (A. G.). Note on Rabies Fixed Virus as an Antigenic Agent when Inactivated by the Photodynamic Action of Methylene Blue. —*Indian J. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 557-560.

⁸ SANKARAN (G.) & BEER (W. A.). The Effect of Exposure of Suspensions of Rabies-infected Brain to Radiation from a Quartz Mercury Vapour Lamp. —*Indian J. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 581-594. With 2 figs. on 1 plate. [13 refs.]

⁹ LEVADITI (C.). Etude de la "neuroprobasie" des virus de l'herpès et de la rage, au moyen du rayonnement total de la lampe à mercure.—*Bull. Acad. Méd.* 1935. Jan. 29. 99th Year. 3rd Ser. Vol. 113. No. 4. pp. 127-139. With 2 figs. [25 refs.]

¹⁰ LIMA (Queiroz). A transmissão da raiva dos herbívoros pelos morcegos hematóphagos da família Desmodontidae.—*Rev. Depart. Nac. da Produção Animal*. Rio de Janeiro. 1934. Vol. 1. Nos. 2, 3 & 4. pp. 165-173. With 11 figs. & 1 folding diagram. English summary.

¹¹ REMLINGER (P.) & BAILLY (J.). Contribution à l'étude du virus de la maladie d'Aujeszky.—*Ann. Inst. Pasteur*. 1935. Feb. Vol. 54. No. 2. pp. 149-184.

blood, sometimes in the nervous system. It is more frequently found in the spleen, the liver, the testicle, the suprarenals, and the bone marrow than is the virus of rabies. The saliva, bile, urine and faeces are never infective. The virus is highly resistant to desiccation, but is destroyed by heating at 60°C. for 50 minutes. It is well preserved in glycerine. It passes L1, L2 and L3 Chamberland, but not Berkefeld V bougies. It is not brought down by centrifugation, and is highly diffusible. For diagnostic purposes the author recommends the rabbit and the cat.

In a long article copiously illustrated BRAGA and FARIA¹² cover much the same ground. Their results, from original observations, need not be recapitulated. It is an admirable summary of the features of the disease and well worthy of study.

A short "text book" description of pseudo-rabies is also given by GENTILUCCI.¹³

A description of pseudo-rabies as it occurs in Spain is given by STEINER and LÓPEZ.¹⁴ Organs from 10 cases were examined, and the conclusion arrived at that the disease exists as an epizootic amongst the cattle of that country.

ii. Symptomatology and Diagnosis.

An interesting case of paralytic rabies simulating an ascending paralysis of the Landry type is reported by DOROLLE, CHAUSSINAND and TRAN-VAN-TAM.¹⁵ The patient came to hospital at Saigon, 33 days after having been bitten on the thumb by a dog suffering from furious rabies. The patient had experienced pain in the bitten thumb and the corresponding arm for 3 days previously. He drank with difficulty, and pharyngeal reflexes were rather exaggerated. He was given antirabic treatment by the dried cord method, and intravenous injections of "sommifene." Five days after admission paresis of the lower limbs became evident, reflexes were abolished, and constipation and retention of urine set in. The paralysis gradually ascended and on the 13th day the diaphragm became involved, and the patient died from cardiac syncope. Appearances of encephalitis were observed post-mortem, but no Negri bodies were found in the horn of Ammon. Two rabbits inoculated died of rabies, after an incubation of 14 days.

The case was characterized by the absence of spasm, by the long duration after symptoms had set in, and by their ascending paralytic nature.

For the rapid diagnosis of rabies by animal experiment WEBSTER and DAWSON¹⁶ recommend the following procedure. A portion of the

¹² BRAGA (Americo) & FARIA (Ascanio). Paralysis bulbar infectuosa (pseudo-raiva, "peste de coçar," doença de Aujeszky). (Terceira nota.)—*Rev. Depart. Nac. da Produção Animal*. Rio de Janeiro. 1934. Vol. 1. Nos. 2, 3 & 4. pp. 53-124. With 27 figs. [65 refs.] English summary (2½ pages).

¹³ GENTILUCCI (Anton Stefano). La pseudo-rabbia (paralisi bulbare infettiva).—*Ann. d'Igiene*. 1935. Jan. Vol. 45. No. 1. pp. 48-53. [23 refs.]

¹⁴ STEINER (A.) & LÓPEZ (C.). Descubrimiento de la enfermedad de Aujeszky en España.—*Rev. Higiene y San. Pecuarias*. 1935. Apr.-May. Vol. 25. No. 4-5. pp. 330-334. [22 refs.]

¹⁵ DOROLLE, CHAUSSINAND (R.) & TRAN-VAN-TAM. Un cas de rage paralytique à évolution lente (paralyse ascendante type Landry).—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 78-81.

¹⁶ WEBSTER (L. T.) & DAWSON (J. R.), Jr. Early Diagnosis of Rabies by Mouse Inoculation. Measurement of Humoral Immunity to Rabies by Mouse Protection Test.—*Proc. Soc. Experim. Biol. & Med.* 1935. Jan. Vol. 32. No. 4. pp. 570-573.

horn of Ammon is emulsified and injected intracerebrally and intraperitoneally into mice. After 5 to 8 days the mouse is killed and smears from the cornu ammonis are examined for Negri bodies.

iii. Pathology.

Using the staining method of MUROMZEFF (smears: 1-2 hours fixation in methyl alcohol: 10-15 minutes in a 2 per cent. dilution of Mann's strain: without washing 10 minutes in 10 per cent. tannin: a few seconds in abs. alcohol: dried Negri bodies bright violet on a pale blue ground), PALAWANDOW, SEREBRENNAJA and PUGATSCH¹⁷ were able to demonstrate the presence of Negri bodies in 100 per cent. of mice, dogs, marmots and hedgehogs, in 80 per cent. of rats and in 75 per cent. of guineapigs infected with fixed virus. In rabbits the percentage was 35 with Kieff fixed virus, 61 with Odessa fixed virus, and 78 per cent. with Sassari fixed virus. They do not regard the power of fixed virus to develop Negri bodies as a reversibility towards street virus since the features of the illness were those of ordinary fixed virus infection.

From photographs taken with infra red rays GUARDABASSI¹⁸ finds that Negri bodies have a granular or filamentous structure; the granules appear usually to be oriented with regard to a point on the periphery. These morphological appearances lead to the view that the body is not the result of a cellular reaction against the virus, but is rather an organic complex, probably a stage in the cycle of evolution of a microorganism.

MATSUDA¹⁹ has continued his observations on the intestinal changes in the rabid rabbit (see this *Bulletin*, Vol. 32, p. 177). The first part of this communication deals with the pathology of the intestinal canal, and the appearances of an acute enteritis are described. These were localized mainly to the portion of the canal between the duodenum and the ileum. The second part deals with symptomatology. A rise of temperature was observed two days before the onset of paralysis. This was accompanied by a slight fall in body weight, by diarrhoea, rhinorrhoea and salivation.

JONNESCO²⁰ cites the case of a dog which after having resisted intraocular inoculation of a strain of a reinforced virus J, received in succession nine intracerebral inoculations of 1 cc. of a 1 in 50 dilution of fixed virus. He concludes that the dog had a natural immunity. After the 4th inoculation, one part of its serum neutralized 9 parts of an emulsion of fixed virus; after the 6th inoculation it neutralized

¹⁷ PALAWANDOW (Haydar), SEREBRENNAJA (A. I.) & PUGATSCH (E. M.). Ueber das Vorkommen und die Eigentümlichkeiten der Negrikörper bei virus fixe.—*Ztschr. f. Hyg. u. Infektionskr.* 1934. Dec. 22. Vol. 116. No. 5. pp. 433-438.

¹⁸ GUARDABASSI (M.). Sur la structure des corps de Negri dans les photomicrographies à l'infrarouge.—*C. R. Soc. Biol.* 1935. Vol. 118. No. 6. pp. 559-561. With 5 figs.

¹⁹ MATSUDA (Shoitsu). The Contribution on the Knowledge of the Experimental Rabies (Report II). I. Pathological Study on the Intestinal of the Hydrophobic Rabbit. II. Study on the Clinical Symptoms of the Hydrophobic Rabbits.—*Oriental Jt. Dis. Infants.* 1934. Sept. Vol. 16. No. 2. [In Japanese. English summaries pp. 12-15.]

²⁰ JONNESCO (Démètre). Recherches sur l'immunité naturelle du chien contre la rage et sur les neurotoxines.—*Ann. Inst. Pasteur.* 1934. Dec. Vol. 53. No. 6. pp. 664-680. With 1 fig. [25 refs.]

19 parts. A small fragment of brain was extracted after the 4th intracerebral inoculation and was found to be infective; a portion of sub-maxillary gland excised at the same time did not contain the virus. A continued increase in the number of eosinophils in the blood was also observed. The authors consider the degree of eosinophilia to be an indication of the degree of immunity. The virus was also shown to be present in the blood serum 17 days after the 4th intracerebral inoculation. In the second part of this paper JONNESCO finds that sensitization by inoculation of a neurotoxic serum lowers resistance to intracerebral inoculation of rabies. Of 13 guineapigs so sensitized, 3 were paralysed in 12 hours, 1 in 6 hours, and 8 between 3 and 7 days, after intracerebral inoculation with fixed virus; whilst 4 rabbits all became paralysed on the following day. These observations are further discussed in a subsequent paper.²¹ A neurotoxic serum was prepared by giving a dog 3 intracerebral inoculations at 8 days intervals of an emulsion of normal dog's brain. This produced similar effects to those above described. Control experiments showed that normal brain substance had no noxious effect upon previously sensitized animals. Thus the author concludes that the paralysis observed in sensitized animals was occasioned by the rabies virus, which diffuses and multiplies much more rapidly when nerve cells have been sensitized by a neurotoxin.

iv. Methods of Treatment and Statistics.

From a series of experiments on rabbits BAKI²² concludes that immunity first appears, after treatment by Högyes' method, between the 11th and 20th day, and lasts for at least 5 months. In the case of those treated by Fermi's method it appears on the 10th day and is still complete after 2½ months. In the case of those treated by Alivisatos' method it appears on the 10th and is still complete after 2 months. In general animals which have been immunized intraperitoneally retained their immunity longer than those treated by intramuscular, intravenous or subcutaneous injections. Rabicidal substances were present in the serum by the 10th day after treatment by each of the three methods, and lasted longer than the immunity. In certain cases when the serum was rabicidal the animal was not immune, and in others when the animal was immune the serum was not rabicidal. The author concludes that the determination of the rabicidal power of the serum is not such a direct indication of immunity as the protection test. [It should be remarked that these conclusions are based upon experiments on 12 rabbits treated by Högyes' method, 6 rabbits treated by Fermi's method, and 6 by Alivisatos' method.]

SHORTT, MCGUIRE, BROOKS and STEPHENS²³ have carried out a series of experiments on methods of immunization against rabies.

²¹ JONNESCO (Démètre). Résistance à la rage des animaux sensibilisés par le sérum neurotoxique.—*C. R. Soc. Biol.* 1935. Vol. 118. No. 15. pp. 1657-1658.

²² BAKI (Sabri). Vergleichende Untersuchungen ueber verschiedene Immunisierungsverfahren bei Wut.—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1934. Sept. 18. Vol. 83. No. 3/4. pp. 184-196. [17 refs.]

²³ SHORTT (H. E.), MCGUIRE (J. P.), BROOKS (A. G.) & STEPHENS (E. D.). Anti-Rabic Immunization: Probable Lines of Progress in Improvement of Methods.—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 537-556.

(1) In the first place they prepared a serum in the sheep and in the buffalo of such a titre that "in a 1 in 5 dilution it was capable of completely fixing not less than 8 minimum haemolytic doses of complement." (2) They then showed in a comparative experiment in which the various protein fractions of the serum were kept in contact *in vitro* with fixed virus that the rabicidal factors were in highest concentration in the euglobulin fraction of the serum. Thus with unconcentrated serum 5 out of 8 rabbits died of rabies, with the euglobulin fraction none out of 8, with the pseudoglobulin fraction 1 out of 8, and with the combined globulins 2 out of 8 died of rabies. (3) It appeared from another experiment that antirabic serum as an adjunct to treatment by carbolized vaccines, when given on the last two days of a 14-day treatment increased the mortality, whilst if given on the first two days the mortality was unaltered, though the average period of incubation was lengthened. (4) An attempt was then made to reduce the mortality of very severely bitten human cases by giving 20 cc. of antirabic serum on the first and second days in addition to the usual course of carbolized vaccine treatment. With serum in addition 7 out of 203 died of rabies (3.44 per cent.) and in the control set with vaccine alone 3 out of 67 (4.48 per cent.) contracted the disease. A confirmatory test was made on a group of persons bitten as described in Hempt's Class IV; of those receiving serum+vaccine 5 out of 381 died, of those receiving only vaccine 4 out of 127 died. The combined results of these two experiments are as follows:—

	Number treated	Deaths	Mortality
Serum + vaccine	584	12	2.05
Vaccine only	194	7	3.60

[This result does not indicate a significant difference between the two methods of treatment.]

(5) In the next section of this paper the authors, following the procedure of FINDLAY for immunization against yellow fever, estimated the value of a single dose of live vaccine+antiserum in immunizing against rabies. The results of two consecutive experiments may be combined as follows. Of 40 monkeys treated with 1 cc. unconcentrated serum plus 0.5 cc. of a 10 per cent. live fixed virus 11 died of rabies (27.5 per cent.) after subsequent infection with street virus; of 41 treated with 1 cc. of combined globulins plus the same dose of live virus 8 (or 20.5 per cent.) succumbed; of 40 treated with 1 cc. of euglobulins plus the same dose of live vaccine 6 (15 per cent.) died of rabies; of 39 treated with 1 cc. of pseudoglobulins plus live virus as before, 8 died of rabies (22.2 per cent.); of 37 treated with the same dose of live vaccine alone 5 contracted rabies (14.2 per cent.), whilst of 42 untreated control monkeys 26 (61.9 per cent.) died of rabies. The authors conclude that such a dose of vaccine+antiserum has a considerable immunizing value although the main effect appears to have been exerted by the live virus, the serum being used mainly to render the use of the live virus more safe. (Thus the numbers of monkeys which died of rabies prior to the inoculation of the infecting dose, were in the successive groups, 2, 1, 2, 3, 5, so that live vaccine alone caused

up to 5 deaths out of 42 monkeys, whilst when treated with antiserum, the numbers averaged 2 out of the same number.)

(6) Finally the effect of following a 7 days course of treatment by carbolized vaccine (10 cc. daily for large dogs, and 5 cc. daily for smaller dogs of a 6 per cent. vaccine) by a dose of 5 cc. of a 1 per cent. dilution of living Paris fixed virus after three weeks and a second 10 cc. dose after a further week's delay, in immunizing against a test dose of 1st passage street virus administered 10 days later, yielded the result that of 8 dogs so treated all escaped, whilst of 8 control dogs all died of rabies [a result of high significance]. The authors conclude that "future lines of advance towards an efficacious means of producing a solid immunity against rabies will be along a path of utilization of antirabic serum and fresh live fixed virus, possibly combined with the use of a dead vaccine."

Statistics regarding the results of treatment at Bandoeng (Dutch East Indies) are published by VAN STOCKUM.²⁴ These are of a very striking nature and will give those who are engaged in the administration of antirabic treatment much food for thought. VAN STOCKUM claims that "each treatment with the Högyes' method and this antigen guarantees almost absolute protection against cases of hydrophobia with an incubation period of more than 30 days." The antigen referred to is described as Monkey Brain (1st subpassage *Macacus cynomologus*); the total dosages at present employed are 212 mgm. over 30 days for Europeans and 407 mgm. over 25 days for natives.

The effect of treatment upon the incubation period has been examined by a number of workers; some believe it to lead to a prolongation of the average incubation period, some to a shortening. The question is a complicated one; on the one hand, one would imagine that the effect of treatment would be to lop off long incubation periods, whilst, on the other, the onset of symptoms might be delayed in those whom treatment fails to cure. These two influences would operate on the average incubation period in contrary directions; the former would tend to shorten it, the latter to prolong it. Some years ago, from an examination of the periods of 282 fatal cases which occurred at Kasauli during the period 1912-1916, by comparing the incubation periods of those who commenced treatment during the 1st, 2nd and 3rd weeks after the bite, the reviewer believed that the effect of early treatment was to prolong the incubation period. This result is, however, not borne out in later statistics. It may be that the average incubations of those arriving during the various weeks are probably not so much a measure of the efficiency of treatment as an indication of the various influences which determine earliness of arrival, and these may vary from institute to institute. VAN STOCKUM claims that Monkey Brain vaccine lops off long incubations and has found no indication that the incubations of those who ultimately die are influenced one way or the other.

The results of the Bandoeng experience in the cases of those arriving during the 1st week may be tabulated as follows:—

²⁴ VAN STOCKUM (Maria J.). New Principles of Antirabic Treatment and Rabies Statistics. A Statistical and Experimental Study. Vol. 1. 204 pp. 1935. The Hague: Martinus Nijhoff. [15s.]

TABLE I.

I = Pasteur method 1895-1905.

II = Högyes rabbit brain 1906-1908.

III = Högyes rabbit brain 1909-1916.

IV = Högyes monkey brain 1916-1932.

	Number treated	Deaths		Proportion of deaths <30 days to total (per cent.)	Mortalities		
		Total	incubation <30 days		Total	incubation <30 days	incubation >30 days
HEAD I ...	164	29	24	83	17.68	14.64	3.05
II ...	80	15	8	53	18.75	10.00	8.75
III ...	249	27	24	89	10.84	9.64	1.20
IV ...	253	20	19	95	7.91	7.51	0.40
ARM I ...	632	16	4	25	2.53	0.63	1.90
II ...	336	15	5	33	4.46	1.49	2.98
III ...	1,101	21	13	62	1.91	1.18	0.73
IV ...	1,074	8	8	100	0.75	0.75	0
LEG AND TRUNK I	593	20	2	10	3.37	0.34	3.03
II	281	6	1	17	2.13	0.36	1.78
III	1,120	8	2	25	0.71	0.18	0.54
IV	1,426	4	4	100	0.28	0.28	0
LIMBS I ...	1,225	36	6	17	2.94	0.49	2.45
II ...	617	21	6	29	3.40	0.97	2.43
III ...	2,221	29	15	52	1.31	0.68	0.63
IV ...	2,500	12	12	100	0.48	0.48	0
ALL POSITIONS I ...	1,389	65	30	46	4.68	2.16	2.52
II ...	697	36	14	39	5.17	2.01	3.16
III ...	2,470	56	39	70	2.27	1.58	0.69
IV ...	2,753	32	31	97	1.16	1.13	0.04

From this table it will be seen that the percentages of deaths with incubations of less than 30 days to the total deaths with monkey brain virus treatment, is in the case of those bitten on the arm 100, in the case of those bitten on the leg it is also 100, and in the case of those bitten on the head 95. These percentages are much higher than those obtained by other methods of treatment at Bandoeng and, so far as I have been able to find from an extensive examination of statistics, at other institutes. In the case of those bitten on the head where incubations are short, the differences are not so striking, but in the case of those bitten on the arm and leg, where incubations tend to be prolonged, cases of long incubation appear to have been absolutely excluded. This result is of high statistical significance and demands careful consideration.

During the years 1925-1930 at Bandoeng a series of alternate cases were treated by carbolized virus and by living monkey brain virus. The results for persons arriving for treatment within the first week after the bite are given in Table II.

TABLE II.

Alternate case experiment, 1925-1930.

		Number treated	Deaths		Proportion	Mortalities		
			Total	Incubation < 30 days		Total	Incubation < 30 days	Incubation > 30 days
HEAD	C.V.	52	3	3	100	5.20	5.20	0
	M.Br.	59	5	5	100	8.50	8.50	0
LIMBS	C.V.	718	6	2	33	0.84	0.28	0.56
	M.Br.	690	2	2	100	0.29	0.29	0
ALL POSITIONS	C.V.	770	9	5	55	1.17	0.65	0.52
	M.Br.	749	7	7	100	0.93	0.93	0

The frequency distribution of incubation periods for those bitten in all positions is as follows :—

	15 days	16-20 days	21-25 days	26-30 days	31-35 days	36-40 days	41-45 days	Totals
M.Br.	0	1	3	3	0	0	0	7
C.V.	1	3	0	1	2	1	1	9

On the assumption that the distributions are random samples of the same population, differences equal to or greater than those observed would be expected in 1 or 2 cases out of 10.

Again the distributions of intervals between the time of commencing treatment and onset of symptoms are :—

	15 days	16-20 days	21-25 days	26-30 days	31-35 days	Totals
M.Br.	1	2	4	0	0	7
C.V.	2	2	1	2	2	9

and the probability is in this case about 0.4. Thus, although the result of this experiment is in agreement with the Bandoeng experience cited above, viz., that deaths with incubation periods of over 30 days have been excluded by treatment by Monkey Brain virus and are not excluded by carbolized vaccines, yet the numbers used were too small for the test to be crucial and the thesis is not proven. The author, however, interprets the experiment differently. She writes " From these statistics it appears again how little stress may be laid on the results obtained in wounds of the head and face for the evaluation of a method as, in both groups, only cases with short incubation periods occurred. The mortality rate of this category treated with live vaccine

was even higher than in the other group ($5/59=8.5$ per cent. against $3/52=5.8$ per cent.). Notwithstanding the available statistical material being but small, the comparison between the results of treatment of wounds of the limbs may be considered as conclusive. For this category all cases of hydrophobia treated with live vaccine fall within the first month after the bite, against only 2 out of 6 ($=33.3$ per cent.) of the other group, in which moreover 2 failures were recorded (36 and 43 days after the bite and 33 and 34 days after commencement of treatment). The exactly identical mortality rate within the first month after the bite in both groups gives evidence of their similar concentration, as could be expected from the method of compilation. It is obvious that all cases observed among wounds of the limbs after the first month should have escaped infection [death] if they had all been treated with live vaccine. In that case, the mortality rate of this category would have been reduced to one-third of the actual mortality rate. Though the results of treatment with such a carbolized vaccine probably compare favourably with those by the Pasteur method and perhaps even with the Högyes' method with rabbit brain fixed virus, this experiment has undeniably pointed out that an entire substitution of the live vaccine by this dead vaccine remains out of the question." It is unfortunate that this experiment was not continued. A definite conclusion on an alternate case basis would have been of the greatest value.

The figures of the alternate case experiment may be further examined. In the fifth column of Table II are given the mortalities according to the different positions for the two methods of treatment. It is at once apparent that the total mortalities for the two methods are very similar (1.17 and 0.93 per cent.). The most striking difference in mortality is in the case of those bitten on the limbs (0.84 per cent. for C.V. as compared with 0.29 per cent. with Monkey Brain virus). This difference, however, is not significant ($P=0.18$). It will also be noticed that the rate 0.29 per cent. for those treated by Monkey Virus in the alternate case experiment is considerably lower than the rate 0.48 per cent. observed at Bandoeng during the period 1916-1932, when Monkey Brain virus was used (see Table I). Again, this difference is not a significant one, but this is in harmony with the statement above that the differences observed during the alternate case test are such as might have occurred as a result of random sampling. It would thus appear that so far as mortality rates are concerned neither the total figures nor those relating to particular positions furnish any definite evidence of superiority of the Monkey Brain virus over carbolized virus.

Thus VAN STOCKUM's conclusion that "since the action of carbolic acid in such a concentration as to ensure an absolutely innocuous vaccine largely deteriorates the antigenic properties of fixed virus, this disinfectant should not be retained for the preparation of dead fixed virus vaccine" cannot be deduced from the facts which she has presented.

On the other hand, as stated above, amongst those treated with C.V. four cases with incubations between 31 and 45 days occurred, whereas with Monkey Brain virus, there were no cases with incubations exceeding 30 days. Although this result is not statistically significant in the alternate case experiment as shown above, it is in conformity with VAN STOCKUM's contention, deduced from her wider experience, that with Monkey Brain virus cases of long incubation are eliminated,

and also with the well-known fact that with C.V. [and so far as I am aware all other methods of antirabic treatment] these cases of long incubation undoubtedly occur.

It remains for the future to show whether with the vaccine employed at Bandoeng the elimination of cases of long incubation will be maintained. In the meantime, the time is clearly ripe for the performance of a crucial test either on animals or on man to elucidate this important point.

The second part of this book is devoted to a study of the etiology and diagnosis of accidents of treatment. The author believes that normal brain substance is absolutely innocuous, and that fixed virus as such is the exclusive cause of accidents. "When treatment with vaccines prepared with virus submitted to heat or to disinfectants with the object of killing, gives rise to accidents, such vaccines are proved still to contain live virus."

The fifth analytical review of reports from Pasteur Institutes prepared from schedules submitted to the Health Section of the League of Nations (McKENDRICK)²⁵ deals mainly with statistics relating to the year 1932. The number of persons treated was 115,959, of whom 439 contracted the disease, and 22 suffered from post-vaccinal sequelae. In previous reviews it was pointed out that there was a marked difference in the mortalities of Europeans and non-Europeans, and that in order to obtain figures which were comparable these race types had been treated separately. It now appears as if the European group was in itself heterogeneous. Disturbances in the form of excessive mortalities are appearing, which have their origin in the Balkan Peninsula, and are independent of the method of treatment employed. The figures suggest that, as regards degree of risk, the Balkan group takes an intermediate position between the European and the non-European. A remarkable fact which has emerged is that amongst those bitten on the leg and treated by killed ether vaccines in Yugoslavia no deaths have been reported amongst 18,152 persons treated over the period for which statistics are available. The figures when divided according to race type show a marked similarity in the mortality rates which occur amongst those treated by the different methods. The same statement holds with regard to the statistics of the U.S.S.R. which are separately analysed.

SÁIZ MORENO²⁶ reviews various aspects of rabies epidemiology, and discusses in particular treatment by SEMPLE's modification of FERMI's vaccine. He concludes that it is innocuous, efficacious and easier of application than other vaccines.

v. Rabies in Animals.

A remarkable increase in the incidence of rabies in South Africa, not only in the *Viverridae*, but also in human beings and in domestic animals is reported by NEITZ and THOMAS.²⁷ (For previous reports see

²⁵ MCKENDRICK (A. G.). A Fifth Analytical Review of Reports from Pasteur Institutes on the Results of Anti-Rabies Treatment.—*Quarterly Bull. Health Organisation, League of Nations*. 1934. Dec. Vol. 3. No. 4. pp. 613-653.

²⁶ SÁIZ MORENO (Laureano). Consideraciones acerca de la epidemiología de la rabia y del poder inmunológico de la vacuna semple.—*Rev. Higiene y San. Pecuarias*. 1935. Apr.-May. Vol. 25. No. 4-5. pp. 335-347. [21 refs.]

²⁷ NEITZ (W. O.) & THOMAS (A. D.). Rabies in South Africa. Occurrence and Distribution of Cases during 1933.—*Onderstepoort J. Vet. Sci.* 1934. Oct. Vol. 3. No. 2. pp. 335-342. With 1 folding map.

this *Bulletin*, Vol. 28, pp. 742-743, Vol. 30, p. 576, and Vol. 31, p. 149.) New outbreaks are reported in the Transvaal and in the Orange Free State.

BOUVIER²⁸ describes cases of rabies amongst dogs in the Congo. These are usually of paralytic type. The number of persons bitten is small, and no fatal human cases have been recorded. Subpassage into guineapigs is usually successful, but in no case have Negri bodies been observed.

vi. Post-Vaccinial Paralyses.

REMLINGER,²⁹ using as his text the reports of 6 cases treated by PASTEUR, which PASTEUR's opponents claimed to be "rage laboratoire," discusses the means by which death from street virus can be differentiated from death from fixed virus. Of the 6 cases above mentioned he believes that three were ordinary rabies, one a case of uraemia and two are indeterminate from lack of evidence. He believes, in spite of affirmations to the contrary, that it is right to attribute a death to fixed virus, if by animal experiment the latter can be demonstrated to be present in the brain. It is not, however, possible to obtain a clear cut differentiation between fixed virus rabies and certain reinforced strains of street virus, though Negri bodies and other histological appearances may aid. Cases of "rage laboratoire" after dried cord treatment, are only observed if the more virulent cords have been injected too early or in too great quantity—that is to say if the long preparation with doses of inoffensive cords advocated by PASTEUR has been neglected. He presses the point that the attenuation of fixed virus for man, ought not to be exaggerated. The large number of passages renders the virus more sensitive to drying and to the action of glycerine, but much less to dilution. This accounts for the greater frequency of "rage laboratoire" amongst persons treated by dilution methods.

A case of paralytic accident presenting the features of the Landry syndrome is described by MARINESCO and FAÇON.³⁰ Symptoms appeared on the 6th and disappeared after a month. The authors recapitulate the various views regarding the causation of such accidents and conclude that they result from a local diminution of the immunity of the nerve substance due to the cytotoxic action of the heterotype vaccine, and, consequently, from a receptivity for neurotropic viruses which up to that time had been deprived of virulence.

A case of death from an encephalo-myelitis occurring after a course of treatment is described by MARINESCO and DRAGANESCO.³¹ Treatment was commenced on the 4th day and completed on the 13th. Symptoms of paraplegia of the Landry type appeared on the 13th day

²⁸ BOUVIER (G.). Mukupa : rage canine congolaise ? (Lomani-Kasai).—*Bull. Soc. Path. Exot.* 1934. Nov. 14. Vol. 27. No. 9. pp. 821-825. [12 refs.]

²⁹ REMLINGER (P.). Pasteur et la rage de laboratoire.—*Bull. Acad. Méd.* 1935. Jan. 8. 99th Year. 3rd Ser. Vol. 113. No. 1. pp. 13-27. [23 refs.]

³⁰ MARINESCO (G.) & FAÇON (E.). Contribution à l'étude de la pathogénie et du mécanisme de production des accidents consécutifs au traitement antirabique.—*Bull. Acad. Méd.* 1935. Feb. 5. 99th Year. 3rd Ser. Vol. 113. No. 5. pp. 169-174. [15 refs.]

³¹ MARINESCO (G.) & DRAGANESCO (State). Recherches anatomo-cliniques et expérimentales sur un cas d'encéphalo-myélite rabique survenue au cours d'un traitement pasteurien.—*Ann. Inst. Pasteur.* 1935. Mar. Vol. 54. No. 3. pp. 299-324. With 10 figs. [11 refs.]

followed by death 6 days later. A full histological description of the brain is given. (No Negri bodies were found.) At the same time rabbit tests were carried out, and in each case paralysis appeared in 4 to 5 days. Possibly this was a reinforced virus.

vii. Miscellaneous.

It may be remembered that PROCA, BOBES, and JONNESCO³² found that antirabic serum was ineffective as a therapeutic agent in the case of mice infected in the tail. This was believed to be due to the richness of the tail in nerve endings (this *Bulletin*, Vol. 31, p. 642). They have repeated the experiment using a finer needle for the introduction of the test dose, and centrifuging the emulsion in place of straining it. In this case the antirabic serum was effective. Of the treated 18 out of 41 succumbed, whilst of the controls 23 out of 32 developed rabies.

HOYT, FISK, and THIENES³³ have continued their researches on the effects of various drugs upon the course of rabies infection (this *Bulletin*, Vol. 28, p. 752). They have now examined the effects of plasmoguin merthiolate, metaphen, bismuth violet, iodobismutol, bismarsen, tryparsamide, silver tryparsamide, Bayer 205, ethyl-hydrocupreine hydrochloride (optochin), pyridium, sodium arsanilate (atoxyl), neostam and sparteine sulphate. "The mean period of incubation and mean length of life (after injection of fixed virus) were calculated for each group. Neither of these periods differed significantly as between the treated and control groups of mice included in any one series of experiments." Thus they conclude that "no evidence was shown that any drugs employed under the experimental conditions described here had any effect whatsoever on the course of rabies produced by injection of fixed virus in white mice."

REMLINGER and BAILLY³⁴ discuss the decentralization of antirabic treatment. They consider it to be an important line of progress. "In this progress, the mother country of Pasteur ought to do what she can, as already other countries have done, for the profit of the nations."

MANOUÉLIAN³⁵ has turned his attention to Borna's disease. Just as in the case of rabies, the inclusion bodies of Borna's disease (the bodies of JOEST DEGEN) are found in the neurones of the central nervous system, and in those of the salivary glands, the pancreas, the suprarenals, etc. They are also present in the intra-glandular and intra-muscular nerve cells of the tongue and in the neurones of its mucosa.

A. G. McKenrick.

³² PROCA (G.), BOBES (S.) & JONNESCO (D.). Sérovaccination et sérothérapie de la rage chez la souris.—*C. R. Soc. Biol.* 1935. Vol. 118. No. 7. pp. 729-732.

³³ HOYT (Anson) FISK (Roy T.) & THIENES (Clinton H.). Experimental Rabies in White Mice and Attempted Chemotherapy, II.—*Jl. Infect. Dis.* 1935. Jan.-Feb. Vol. 56. No. 1. pp. 21-27. With 1 chart.

³⁴ REMLINGER (P.) & BAILLY (J.). La décentralisation de la vaccination antirabique.—*Bull. Acad. Méd.* 1935. May 7. 99th Year. 3rd Ser. Vol. 113. No. 17. pp. 579-583.

³⁵ MANOUÉLIAN (Yervante). Rage, maladie de Borna et neurones périphériques.—*C. R. Acad. Sci.* 1935. Mar. 4. Vol. 200. No. 10. pp. 862-863.

HELMINTHIASIS.

- YAO (Y. T.), HSU (S. C.) & LING (S. C.). **On the Occurrence of Intestinal Parasites in Man in Different Combinations. (A Statistical Study of the Results of 9,853 Fecal Examinations.)**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 531–538.
- , — & —. **Intestinal Parasite Infestation of Primary School Children in Nanking. (A Record of Survey from April 1932 to April 1933.)**—*Ibid.* pp. 539–549. [27 refs.]
- & CHU (H. J.). **Intestinal Parasites among the People under Suburban Conditions in Tangshan, Nanking.**—*Ibid.* pp. 551–553.
- YU (T. H.), CHU (P. J.), WANG (C.) & TAO (C. S.). **The Prevalence of Intestinal Parasitic Infection among School Pupils in Shanghai.**—*Ibid.* pp. 555–556.

Examination was by 6 smears (3 made with saline solution and 3 stained with iodine-eosin solution) for 2,877 faecal examinations reported on in the second paper, and presumably the same technique was used for the first.

The figures are statistically considered and incidence is of local value. It is particularly noted that little correlation was found between degree of intestinal infection and the child's physical and mental development.

The incidence of infection in 1,365 "school children" between 6 and 20 years of age was investigated. Figures of results are not given. *Fasciolopsis buskii* was present. Tangshan lies 20 miles east of Shanghai.

"Faecal examination" of 1,412 school children at Shanghai showed 48.4 per cent. with parasites, namely *A. lumbricoides* 35.9, *T. trichiura* 22.8, *F. buskii* 1.6, *A. duodenale* 0.6, *C. sinensis* 0.3. Clayton Lane.

- i. VOGEL (H.), WU (K.) & WATT (J. Y. C.). **Preliminary Report on the Life History of Paragonimus in China.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 509–517. With 5 figs. on 2 plates.
- ii. LOUCKS (H. H.). **Hydatid Disease in China.**—*Ibid.* pp. 567–571. With 3 figs. on 2 plates.
- iii. KU (D. Y.) & KAO (Z. M.). **Some Histological Observations on Filariasis Bancrofti.**—*Ibid.* pp. 573–585. With 10 figs. on 5 plates. [12 refs.]
- iv. MINAMIZAKI (Yushichi). **A Study of the Viability of Hookworms in the Intestine.**—*Ibid.* pp. 587–588.
- v. YOSHIDA (Sadao). **Contribution to the Study on *Gnathostoma spinigerum* Owen 1836, Cause of Esophageal Tumor in the Japanese Mink, with Especial Reference to its Life History.**—*Ibid.* pp. 625–630. With 15 figs. on 6 plates.

i. Vogel, Wu and Watt have found encysted metacercariae of paragonimus in *Potamon denticulatus*, apparently the first time they have been seen in this host in China. The infection rate of these crabs varied in 8 infected villages from 4.6 to 27 per cent. The method of eating these is to put them for a few hours in a pot of rice-wine, salt and anise-like spice in which they rapidly die. The soft parts, especially from the legs, are sucked out, and it is in the legs that a

high percentage of cysts has been found. Work is being undertaken to determine how long the cysts survive within crabs lying in this sauce. [See also KHAW below, p. 629].

ii. Loucks reports 3 more cases of hydatid from the Peiping Hospital.

iii. Ku and Kao report on the histology of material from 5 filarial cases. The tissue changes are such as are in fact common, but the writers are evidently unfamiliar with the appearance of the adult worms when seen in tissue sections, and the reproduced photo (Fig. 10) does not permit of the certain identification of what they believed to be a young worm.

iv. Minamizaki by self-infection through the skin put the life-span of "hookworms" as about 7 years.

v. Yoshida reports that 47 per cent. of 5,253 Japanese mink examined were infected with gnathostomes, the lesion being in the lower end of the oesophagus. The eggs when freshly passed are not embryonated, as in fact they were in the preserved material examined by BAYLIS and LANE. The work of PROMMAS and DAENGSVANG (this *Bulletin*, Vol. 30, p. 711) is confirmed, namely that development to the stage of armed head-bulb with 4 cervical sacs and alimentary canal occurs in cyclops. The further course is being investigated.

Ten other helminthological papers presented to the Congress are noted under titles only on pp. 674-675. C. L.

GUY (R.). Parasitisme intestinal à Luang-prabang (Haut-Laos). [*Intestinal Parasites in Upper Laos.*]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Dec. Vol. 12. No. 10. pp. 934-939.

Faecal smears gave the following percentages of infection for school children, military and police respectively.

Hookworms 44, 52·9, 52; trichuris 88, 62·3, 54·8; ascaris 92, 38·8, 52. The prevalence of malaria caused blood examinations for anaemia to bear little relation to helminthic disease. C. L.

i. CHEN (H. T.). *Helminths of Dogs in Canton, with a List of those occurring in China.*—Reprinted from *Lingnan Sci. Jl.* Canton. 1934. Jan. Vol. 13. No. 1. pp. 75-87. With 1 fig. & 1 plate. [15 refs.]

ii. ——. *Helminths of Cats in Fukien and Kwangtung Provinces with a List of those recorded from China.*—*Ibid.* Apr. No. 2. pp. 261-273. [20 refs.]

i. Of the parasites found in 54 dogs, mostly from Canton, the percentages of those directly or indirectly of human interest were: *Clonorchis sinensis* 44·2, *Metagonimus yokogawai* 3·8, *Echinostomum ilocanum* 13·5, *Paragonimus* sp. 1, *Dirofilaria immitis* 13·7, *Dipylidium caninum* 77, and *Diphyllbothrium mansonii* 7·7. The percentage infected with *C. sinensis* is a notable one.

ii. Similarly the finds in 57 Canton cats were: *C. sinensis* 80, *M. yokogawai* 3·51, *D. caninum* 38·6, *D. mansonii* 28·07, sparganum probably of *D. mansonii* 1·75, *Ancylostoma braziliense* 36·84, *D. immitis* 3·51, a strongyloides 1·75. In 32 Foochow cats the corresponding figures were 59·37, 0, 62·5, 15·63, 0, 0, 0, and 0. Again the clonorchis infections were many. C. L.

HILMY (I. S.). The Microscopic Examination of Faeces for Helminthic Infection.—*Jl. Egyptian Med. Assoc.* 1935. Jan. Vol. 18. No. 1. pp. 39-47. [19 refs.]

Various diagnostic methods for detection of helminthic eggs are described; two are compared by the positives they display. These last are Khalil's gravity floatation in an Erlenmeyer flask, which it is reported is in use in all hospitals in Egypt for the mass diagnosis of hookworm infection, and D.C.F., which is wrongly described as an adhesion method [for it is the non-adhesion which it produces that enables its essential herding to be accomplished].

"The following unpublished figures are given with the kind permission of Professor Khalil Bey. They are the result of the examination of 521 cases by this and Khalil Bey's method.

210	were positive by Lane's, or 40.31 per cent. ;
195	" " Khalil Bey's, or 37.43 per cent. ;
32	" " Lane's, but negative by Khalil Bey's ; and
15	" " Khalil Bey's and negative by Lane's.

From the above it is seen that Lane's method gives about 3 per cent. more positives, but it entails the use of an entirely new apparatus."

[This method of comparison is unscientific. The smear will detect every infection if sufficiently heavy.] C. L.

EMARA. Toxicity of Carbon Tetrachloride.—*Jl. Egyptian Med. Assoc.* 1935. Jan. Vol. 18. No. 1. pp. 3-14. With 6 figs.

SHAFY MOH (Abdel). Note on Pathological Findings on a Case of Carbon Tetrachloride Poisoning.—*Ibid.* pp. 15-16.

The symptoms and lesions in a case of fatal poisoning with carbon tetrachloride are described.

A girl of 12 was given 2 cc. of carbon tetrachloride and a purge and enema, and died in 48 hours with vomiting, diarrhoea, jaundice, coma, extensive central necrosis of the liver and advanced cloudy swelling and fatty change in the tubular epithelium of the kidneys. The bowel contents were free from the drug. A second case of Professor DAY's is reported in a man of 55 who died collapsed, 29 hours after taking carbon tetrachloride, the bowels having been well opened; the liver showed multiple foci of necrosis 5 to 30 mm. in diameter. The causes contributing to poisoning are discussed. C. L.

HASSAN (A.) & SALAH (M.). Investigation on Carbon Tetrachloride Intoxication.—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 207-213.

A survey of literature with report on certain experiments.

No cases of poisoning by the drug have in fact occurred in the hospital of the Research Institute, Cairo. The ill effects which occur with ascaris infection were investigated by shaking for 4 hours bits of fresh ascaris from man in carbon tetrachloride in the proportion of 7 to 5. Administration of 5 cc. per kilo of the extract to dogs caused no ill effects, nor did similar quantities of an extract of dried worms. As commonly reported liver function tests were almost or actually negative. The authors' investigations leave them unprepared to agree at the moment that calcium deficiency is an important predisposing factor in poisoning; but during discussion Salah did not

deny the antagonism of tetrachloride and calcium, but held that the success of calcium therapy did not necessarily indicate a previous calcium deficiency. Toxic symptoms occurring within 24 hours of administration appeared to be due to depressed cerebral action and should be treated by enemata, and respiratory and heart stimulants (caffeine and adrenalin). In discussion Professor KHALIL reported that the exact number of cases of "carbon tetrachloride poisoning" was unknown but 7 or 8 were reported yearly by the Parquet.

C. L.

TEICHLER (G.). Ueber die anthelminthische Wirkung der Wurzelrinde von *Vangueria edulis*. [Anthelmintic Action of Root Bark of *V. edulis*.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 211–213.

A decoction of the rind of the root of *Vangueria edulis* was tested against certain intestinal worms.

Edulin, as the decoction is named, was tested in 100 cases against ascaris. It produced passage of worms but the details given do not permit of proper assessment of its value. Threadworms were passed in numbers. In the four cases of hookworm and one of taenia infection in which it was tested there was failure.

C. L.

RATNAGIRISWARAN (Arayapuram Natesa), SEHRA (Kumar Banu) & VENKATARAMAN (Krishnasami). **The Anthelmintic Constituent of the Leaves of *Calycopteris floribunda*.**—*Biochem. Jl.* 1934. Vol. 28. No. 6. pp. 1964–1967.

Calycopteris floribunda (N.O. Combretaceae) grows in Madras, where the young leaves are reputed to have anthelmintic properties. Calycopterin is found to be toxic to round worms. Summary:—

"1. The anthelmintic constituent, *calycopterin*, of the leaves of *Calycopteris floribunda* has been isolated.

"2. Calycopterin is shown to be a dihydroxytetramethoxyflavone, which yields *p*-hydroxybenzoic acid on fusion with alkali.

"3. Demethylation of calycopterin gives a new hexahydroxyflavone, *calycopteretin*."

C. L.

AZIM (M. Abdel). **The Epidemiology and Endemiology of Schistosomiasis in Egypt.**—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 215–226. With 1 fig.

Observations on the distribution and bionomics of bilharzia carriers in Egypt.

In Egypt *Bulinus contortus*, *B. dybowskii* and *B. innesi* live at the bottom of main streams and canals with running water clinging to weeds, for they need much oxygen. *Planorbis* snails are absent from the Nile and big canals and prefer slow moving or stagnant and muddy water. In discussion KHALIL reported thus:—

"*Bulinus* snails have been caused to change from one species to another and to give rise to intermediate species by cross breeding. So, they are not fixed species. In Egypt, we find certain species of *Bulinus* prevailing in certain districts; for example, in the oasis only *Bulinus dybowskii* exists. In Helwan the same species is in great preponderance. From Khartoum to Cairo only *Bulinus* snails exist, while north and south of this zone, both *Bulinus* and *Planorbis* are found. In the Blue Nile, where

the water is very soft, only *Bulinus* snails are present, whereas in the White Nile, where the water has a higher salt content, *Planorbis* is found. It is claimed that the distribution of the various snails is governed by the rapidity of the stream. The pointed snails can withstand the most rapid streams. They can be arranged, according to their resistance, in the following order. *Physa*, *B. innesi*, *B. dybowskii*, *B. contortus*, and *Planorbis*. This can be seen in the river Nabi Robin in Palestine where the water is running very swiftly, yet there are *Bulinus* snails and *Schistosoma haematobium*."

HILMY reported thus :—

"I have been trying to infect *Planorbis* snails experimentally with *Schistosoma haematobium* miracidia. Up to now the development has reached the sporocyst stage in the livers of the snails and I am hoping to obtain the complete development to the cercaria stage." C. L.

VIGLIETTA (Carlo). Osservazioni e ricerche sulla schistosomiasi vescicale dei bambini. [**Urinary Schistosomiasis in Children in Derna (Cyrenaica).**—*Pediatrics*. 1935. Jan. 1. Vol. 43. No. 1. pp. 54–66. [32 refs.] English summary (4 lines).

The author examined 606 children attending the local elementary schools and found 9 of them (1·5 per cent.) with urinary schistosomiasis. Their ages varied between 8 and 13 years. Only one was accustomed to bathe in the Wady, all the others bathed in the irrigation canals. *Bulinus contortus* was common. Of the 9 six presented typical symptoms, one suffered much pain, the other two had never noticed anything unusual or any discoloration of the urine, and blood was found only by microscopical examination. The author strikes a note of warning lest the introduction of these children into Italy should lead to diffusion there. H. H. S.

BERGEROT (Jean). Le foyer de bilharziose de Djanet, Pays Ajjer (Sahara Algérien). [**Focus of Schistosomiasis at Djanet, Algerian Sahara.**—*Arch. Inst. Pasteur d'Algérie*. 1935. Mar. Vol. 13. No. 1. pp. 47–67. With 8 figs. on 4 plates. [10 refs.]

The oasis of Djanet is described as the only focus of schistosomiasis in Algeria. Djanet lies close to the frontier of Tripoli at 24°N. The focus has been known since 1923, and infection is by *S. haematobium*, to the extent of 27 per cent., invasion being accompanied by skin rashes. The snails have been identified as *Bulinus contortus*, *B. dybowskii*, *B. brochii*, and *B. innesi*. The sterilization of pools by copper sulphate is rendered difficult by the springs which feed them, and will require much perseverance. C. L.

CAWSTON (F. Gordon). **Artificial Sources of Schistosome Infection and the Cure of Patients.**—*Jl. Trop. Med. & Hyg.* 1935. May 1. Vol. 38. No. 9. pp. 105–106.

Infective *Physopsis africana* can be excluded from a garden by running the entering water through $\frac{1}{4}$ in. mesh; eggs pass through, but provided the water in the garden is not subsequently infected the adult snails are harmless. That neighbouring pools may have or may not have snails in them shows that birds have little influence in spreading these. The disuse of potassium antimonium tartrate in spreading these. The disuse of potassium antimonium tartrate in spreading these. The disuse of potassium antimonium tartrate in spreading these. C. L.

LUTROT (M.). Note sur deux foyers malgaches de bilharziose vésicale à *Schistosomum haematobium*. [Two Madagascar Foci of Urinary Schistosomiasis].—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 243-245.

S. haematobium has been found in indigenous persons, it is stated for the first time, in two spots in Madagascar, Tsianipiha and Anjijobe.
C. L.

KHALIL Bey (M.). Chemotherapy of Schistosomiasis.—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 284-294.

A useful survey of aspects of the antimonial treatment of schistosomiasis.

Potassium antimonium tartrate has these disadvantages. Local thrombosis, rare even with the concentrated solution used in Egypt; opacity with greatly increased toxicity if boiled till opalescent—probably the oxide is formed; increased toxicity unless freshly prepared—perhaps from the formation of isomers; local inflammation in 5 per cent. of cases—probably from escape of fluid into the tissues; cough in 10 per cent. of cases; nausea and vomiting in 38·8; fever; muscular pains in later stages of treatment. Complications are herpes and dermatitis. Contraindications are put as nephritis, heart failure and fever. Twelve injections were given on alternate days, and continued if a cure was not attained. Cure percentages in 1,000 consecutive cases completing the course were 89·4 in all; after 12 injections 68·3; after 13, a further 10·3; after 14 to 17, a further 10·8. Half the treated did not complete the course.

Sodium antimonium tartrate is less stable than the potassium salt. As to foudadin cases treated may be summarized thus:—

Year	No. of cases	Percentage cured after			Percentage relapsed after 1 month
		9 injections	11 injections	13 injections	
1931	3,288	52·26	15·69	3·31	0·71
1932	2,299	62·20	20·50	4·10	9·30
1933	3,302	63·41	15·23	4·38	12·92

Complications and sequelae are not given in comparable figures. Bradycardia is frequent but unexplained. In 1933, fever occurred in 36 cases and was due to typhoid in 6, pyelitis in 7, malaria in 4, abscess in 1, unexplained 18; oedema in 3; herpes zoster in 4; exacerbation of pellagrous erythema repeatedly; vomiting in 0·36 per cent.; abscess twice in 2,000 cases or 20,000 injections; sudden death once in 2,041 cases. There are also considered the effects of foudadin on the liver, its excretion mainly by the kidney, its injection daily which gave toxic symptoms in half the cases, its use in large doses, and the use of foudadin calcium. The ideal drug will cure in one injection or will be capable of oral administration. In discussion SALAH pointed out the lessened efficiency of foudadin during the last 3 years. C. L.

FAUST (Ernest Carroll), JONES (Charles A.) & HOFFMAN (William A.).
Studies on Schistosomiasis Mansonii in Puerto Rico. III. Biological Studies. 2. The Mammalian Phase of the Life Cycle.—
Puerto Rico Jl. of Public Health & Trop. Med. 1934. Dec.
Vol. 10. No. 2. pp. 133-196. With 3 text figs., 7 charts &
9 figs. on 4 plates. [32 refs.] [Spanish version pp. 197-254.]

For the first time the growth of the worm in the definitive host has been traced in rat, rabbit and monkey from entry of the cercaria to oviposition by the female. Tissue changes in relation to habitat have been described.

Cercariae emitted before 2 p.m. from several *Australorbis glabratus* were pooled to make certain of their being of both sexes. The hosts were examined very thoroughly. Though cercariae are described as being equally distributed through the water, the parts attacked as evidenced by irritation are those at or above the surface level of those wading in water [which suggests pushing against the residual water film as a help in effecting penetration and falls in with the authors' belief that the greater the effort to dislodge the "inoculum" the wider will it be spread]. Penetration is presumably aided by the gland secretions since the glands are almost empty when the larvae are in the dermis. Migration was almost wholly by the blood stream first to the lungs and then to the liver. It is believed from observations every few hours that feeding on blood begins in the liver and that if metacercariae are found with blood in them in the heart or lungs they have been in the liver and been washed out of it back to the lungs. The various stages of growth are labelled with the letters of the Greek alphabet from alpha to omega but in the Summary and Conclusions the sixth letter of the alphabet is spoken of as if it were the fourteenth, the resulting confusion being an added reason for accepting the fact that Greek is learnt by few scientists nowadays and for using only the four stages also mentioned, metacercarial, juvenile, adolescent and adult. From the liver the immature worms go to the mesenteric veins (in the rat about the 23rd day) and make for the veins about the ileo-caecal junction; others crowded out of these spread through the mesenteric, the haemorrhoidal and vesical veins. Mating takes place in these veins, the 47th day being noted as showing worms in copula and eggs in the tissues. Up to the 9th month at least worms in the mesenteric vessels outnumbered those in the liver by 5 to 1 in these overcrowding infections. In these hosts worms in copula were rare. Usually there was 1 egg in the uterus and it is estimated that 100 or more are laid daily, it being held that few per cent. leave the body.

"Increases in young neutrophilic leukocytes (*i.e.*, stab forms, juveniles and myelocytes) were registered (1) during the period of invasion of the larvae through the skin, (2) at the time of their maximum accumulation in the lungs, and (3) with the initiation of oviposition by the mature female worms. These increases were relative and were never accompanied by an absolute leukocytosis.

"There was no local reaction at the sites where the larvae entered the skin. On the other hand, during the passage of the metacercariae through the lungs, and, later, around the sites where eggs were infiltrated into the liver and the intestinal wall, there was first an intense response on the part of the neutrophilic leukocytes, which were replaced by successive invasions of eosinophiles, plasma cells and fibroblasts. Generalized eosinophilia developed in some of the animals toward the end of the prepatent period

and at the beginning of the patent period. Its complete absence in one monkey is to be regarded as a lack of defensive response to the disease, which caused the death of the animal on the 55th day. In general, with the progress of the infection a relative peripheral lymphocytosis developed.

"The degree of anemia in both the experimental and clinical cases was dependent primarily on the severity of the infection rather than on the duration of the disease.

"Only one of the experimental hosts had a positive Sia euglobulin reaction. This did not appear until some days after a significant eosinophilia had been registered. On the other hand, 8 of the 11 human cases examined had a positive euglobulin reaction, but there was no evidence of correlation between the intensity of the euglobulin reaction in the blood and the degree of eosinophilia.

"The hematopoietic response in experimental and human infections of schistosomiasis mansoni is similar to that of other helminthiasis, in which an early acute reaction is followed by gradual adjustment of the host tissues to the invading organism."

C. L.

DE BÈVE (F.). La bilharziose en Ruanda-Urundi et spécialement à Usumbura. [**Schistosomiasis in Ruanda-Urundi.**—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 3-18. With 3 figs.

A study of Mansonian schistosomiasis at Usumbura, the capital of Ruanda-Urundi.

This town lies near the equator on the north-east shore of Lake Tanganyika, which has an altitude of about 2,500 feet. Swampy ground lies beside it, containing many Planorbis and worked over by fishermen of whom over 50 per cent. are infected with *S. mansoni*. The Planorbis emit by day cercariae of human type. Of 120 fishermen examined by means of 2 faecal smears the percentages of infection found were: hookworms 72.2, *S. mansoni* 53.2, trichuris 27.5, ascaris 23.3, strongyloides 22.5, tapeworms 6.7, Giardia 0.8. All were infected by some parasite. In 120 urines no blood, albumin or schistosome eggs were found. Symptoms and physical signs, and the pathological anatomy of an excised rectum are described. Treatment was by tartar emetic and emetine. Prophylaxis is discussed.

C. L.

HULSHOFF (A. A.). **An Extraordinary Case of Schistosomosis mansoni.**—*Acta Leidensia (Scholae Med. Tropicae)*. 1933. Vol. 8. pp. 231-241.

This is reported as the second case of chylothorax caused by schistosomiasis.

The man, a native of Djibouti, was found at Rotterdam to have in the faeces many eggs of *S. mansoni*, oedema of legs and back, ascites, fluid in the left pleura, albuminuria with casts, hyaline granular and waxy. On puncture of the left pleura a chylous fluid escaped. This had to be repeated a number of times and the abdomen had to be tapped several times. He died and the autopsy is held to have disclosed "lymphogenic tuberculosis." Under the pleura lay very many shining white spots, which under the microscope displayed no schistosome eggs but were believed to be tubercles with caseation. Similar spots were seen in liver and spleen. Schistosomes were present in mesenteric veins. [Examination of the night blood is not mentioned.]

C. L.

LEVINE (Jacob) & MARIN (Rafael A.). **Carcinoma and Schistosomiasis of the Appendix. A Case Report.**—*Jl. Lab. & Clin. Med.* 1935. Mar. Vol. 20. No. 6. pp. 602–605. With 3 figs.

A carcinomatous appendix was removed from a Porto Rican woman of 28. It contained encapsuled schistosome eggs in that part only which was carcinomatous. C. L.

CAWSTON (F. G.). **Climatic Changes and their Effect on Fresh-Water Molluscs.**—Reprinted from *Trans. Roy. Soc. South Africa.* 1934. Vol. 22. Pt. 1. pp. 81–82.

The author finds that the prolonged drought in the Union of S. Africa of the last few years has been detrimental to the breeding of pond snails such as *Physopsis africana* Krauss, *Bulinus tropicus* Krauss, *Lymnaea natalensis* Krauss, and that the increase of marsh land in the mountainous districts consequent on shortage of rainfall has favoured the smaller species such as *Lymnaea truncatula* Müller, a carrier of Fasciola. He notes also that the anti-malarial treatment of collections of water near the coast with chemicals has destroyed much of the vegetation on which pond snails breed. A. G. B.

ANDREWS (Mary N.). **The Examination of Faeces for the Ova of Schistosoma japonicum.**—*Chinese Med. Jl.* 1935. Jan. Vol. 49. No. 1. pp. 42–46.

For diagnosis of infection with *S. japonicum* the hatching out of miracidia by the method of Faust and Meleney was found to be the best.

Stools of 76 cases were positive to Faust and Meleney's method. Of them 29 were positive to the smear and 22 more to sedimentation [TOMB and HELMY, this *Bulletin*, Vol. 29, p. 410]. The method of Faust and Meleney does not seem to have been described in this *Bulletin*. Briefly it consists of repeated sieving, washing and gravity precipitation of the whole stool, until the supernatant fluid is quite clear. It is stood all night in a conical Ehrlenmeyer flask and is then examined with a hand lens for miracidia. These of course congregate near the top and the small surface of the neck of the conical flask produces further concentration. C. L.

SAITO (Minami). **Wild Rats in Reference to the Prevention of Schistosomiasis.**—*Jl. Public Health Assoc. Japan.* 1935. Mar. Vol. 11. No. 3. pp. 1–5.

Wild rats in the Kofu valley are heavily infected with *S. japonicum* in villages where liming for the destruction of *Oncomelania nosophora* has not been carried on, and but lightly infected in those where this measure has been used.

In non-limed areas the infection rate of 792 rats caught in winter was 19·17 and of 316 caught in summer was 76·89. In limed areas the winter rate among 228 rats was 2·19, and the summer rate among 90 was 1·11. In winter the rates for man and rat were close to one another, in summer those for the rat were the higher. The average length of male worms in the rat was 1·48 cm. and of females 1·79. Though many eggs in the rat's faeces were degenerate, miracidia from

the others developed in the snail "into the sporocyst and then to the redia." The infection rate according to rat species is given as follows:—

"In the cold season it was 17.94 per cent. for *Microtus montebelli*, 16.77 per cent. for *Apodemus speciosus*, 4.44 per cent. for *Rattus norvegicus*, and 1.54 per cent. for *Mus molossinus*, whilst in summer months it was 64.78 per cent. for *Microtus montebelli*, 58.06 per cent. for *Apodemus speciosus*, and as for *Rattus norvegicus*, none of the 9 rats caught in the intensely infected area was found infected." C. L.

LI (T. Y.) & THOMPSON (H. Gordon). **Treatment of Schistosomiasis Japonica with Antimony Compounds. Review of Literature on Chinese Cases: Report of 15 Cases.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 325–344. [44 refs.]

The paper's scope is shown in the subtitle.

"In establishing criteria of cure in schistosomiasis therefore, we should, for the present, consider all the 4 points together:—

- "(1) Permanent absence of ova from the stools for at least 2 years.
- "(2) Return to normal of eosinophile percentage after other helminths are cleared out.
- "(3) Positive Fairley's test becoming negative.
- "(4) General improvement of health with disappearance of pre-existing symptoms such as: abdominal pain, epigastric discomfort, and dysentery."

"In the matter of treatment, it appears to us that although P.A.T. is a drug which requires a great deal of care in its use, yet properly used it is still the most efficacious remedy for schistosomiasis japonica."

C. L.

KOURÍ (Pedro), BASNUEVO (José G.) & FERMOSELLE BACARDÍ (Joaquín). Poder fasciolicida del clorhidrato de emetina. [**Emetine Hydrochloride in Fasciola Infestation.**—*Medicina Paises Cálidos.* Madrid. 1935. Mar. Vol. 8. No. 3. pp. 145–146.]

The authors are fully convinced of the power of emetine hydrochloride to destroy *Fasciola hepatica*. The average dose to attain this end they find is 3.72 mgm. per kilo body weight.

They mention the case of a woman of 38 years, weighing 43 kilos, who was cured by 16 cgm. and believe that smaller amounts would probably suffice. For an adult of 70 kilos 80 cgm. would be a toxic dose or 11.4 mgm. per kilo, so that the therapeutic coefficient would be about 0.3. Taking the average dose mentioned, a man of 70 kilos would need 260.4 mgm. to effect a cure, which is less than a third of the toxic dose, 800 mgm.

H. H. S.

KOURÍ (Pedro), BASNUEVO (José G.) & ARENAS (Rogelio). Un nouvel emploi d'emetine en parasitologie.—*Crónica Med.-Quirúrg. Habana.* 1934. Oct. Vol. 60. No. 10. pp. 427–430.

—, — & —. [In Spanish & English.] Una nueva aplicación de la emetina en parasitología. **A New Use of "Emetin" in Parasitology.**—*Archivos Med. Infantil.* 1935. Jan.–Feb.–Mar. Vol. 4. No. 1. In Spanish pp. 21–23. In English pp. 24–26.

Six cases are cited in which emetine cured infection with *Fasciola hepatica*.

C. L.

KHAW (O. K.). *In Vitro* Experiments on the Viability and Excystment of *Paragonimus Cyst*.—*Proc. Soc. Experim. Biol. & Med.* 1935. Apr. Vol. 32. No. 7. pp. 1003-1005.

The length of life of *Paragonimus* cysts outside any host and the physical conditions which make for excystment are detailed.

"These experiments demonstrate that in a diluted millet wine containing 10 per cent. alcohol and in rice wine (14 per cent. alcohol), the encysted metacercariae were viable up to 43 and 18 hours at room temperature (22°C.), respectively, and that they could be kept alive in the ice chest (10°C.) in 10 per cent. commercial formalin or in 0.9 per cent. saline for over 3 weeks. Therefore, the customary mode of preparing crabs, as practised by the villagers in the endemic area where the infection rate for crabs varies from 25 to 100 per cent., by soaking them, very often only over night at room temperature so as not to spoil the taste, in a weak solution of salt and yellow rice wine seasoned with spices, cannot kill all the cysts of *Paragonimus*. This would account for the high rate of infection, 87 per cent. in one village, prevailing in the Lan Ting district."

Artificial gastric juice did not help excystment, which occurred in 3½ hours after this was replaced by artificial intestinal juice; it took place in 1½ hours in intestinal juice with bile, in 45 to 90 minutes without bile, in 75 minutes in 12 per cent. bile. There was no excystment in 0.2 per cent. sodium carbonate nor in boiled bile or artificial intestinal juice.

C. L.

RAO (M. Anant Narayan). *Lung Flukes in Two Dogs in the Madras Presidency*.—*Indian Jl. Vet. Sci. & Animal Husbandry.* 1935. Mar. Vol. 5. Pt. 1. pp. 30-32. With 3 figs. on 1 plate.

The author reports lung flukes identified as *Paragonimus westermanii* from a dog in Malabar on the west coast of the Madras Presidency, another from adjoining Coimbatore, and a third from a panther shot at Coorg adjoining Malabar.

C. L.

CHEN (H. T.). *A Preliminary Note on the Life History of Paragonimus in China*.—Reprinted from *Lingnan Sci. Jl.* Canton. 1935. Jan. Vol. 14. No. 1. pp. 143-144. With 4 figs.

A preliminary report. A figured but unidentified snail and crab are believed for unstated reasons to be the larval hosts of *paragonimus* in China.

C. L.

WAGNER (Oskar). Hautallergie und Komplementbindungsreaktion bei Trematodeninfektionen. [*Skin Allergy and Complement Fixation in Trematode Infections.*]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Feb. 14. Vol. 84. No. 2/3. pp. 225-236. [11 refs.]

A combination of complement fixation and skin reaction was positive in 90 per cent. of cases of infection with *Fasciola hepatica* in sheep, using as antigen an extract of this fluke. Complement fixation with this extract was also positive with *Dicrocoelium*.

C. L.

OTTO (I. H.) & TSCHAN TSCHING JI. Ueber die Behandlung der menschlichen Infektion mit *Clonorchis sinensis* (Kobbold) mit Goldeinspritzungen. (Vorläufige Mitteilung.) [Treatment of Clonorchis Infection in Man with Gold Injections.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 99–106. With 1 fig. [31 refs.]

Gold injections were effective against *C. sinensis*. Two substances were used, Solganal B oil and auroprotasin. They were apparently always injected intravenously.

Solganal B oil was given to 26 patients. The initial dose seems to have been 0.01 cc. but to have been increased to a varying extent. Thus two who had 11 injections each received in all 0.8126 and 2.57 cc. respectively. Of the 26, the eggs were lost in 16, four are still under treatment and six stopped treatment prematurely. With this treatment and liver extract by mouth an existent urobilinoginuria disappeared and did not return on stopping treatment. Auroprotasin was given to 4 persons; one broke off treatment after 6 doses totalling 13 cc. and was uncured, the other 3 were cured. Dosage started at 1 cc. rising to 5 cc. with total dosage of 9 to 30 cc. The Takata-Staub-Jezler reaction is positive in severe cases. C. L.

UYENO (Hiroshi). Ueber den Zucker- und Fettstoffwechsel und die passive Anaphylaxie bei experimenteller Kaninchenclonorchiasis. (I. Mitteilung.) Experimentelle Untersuchung ueber den Zuckerstoffwechsel bei der Kaninchenclonorchiasis. [Sugar Metabolism in Rabbit Clonorchiasis.]—*Okayama-Igakkai-Zasshi (Mitt. d. Med. Gesellsch. z. Okayama)*. 1935. Mar. Vol. 47. No. 3. [In Japanese pp. 674–691. [61 refs.] German summary pp. 673–674.]

The author's conclusions on rabbits infected with clonorchis are as follows. In early and light infections the blood is not notably changed. In heavy cases near the end there is marked increase of sugar content, preceded perhaps by a short lessening possibly correlated with the increased icterus and biliary acids in the blood. When glucose, fructose, or galactose is intravenously injected into gravely ill rabbits, high and lasting hyperglycaemia results, accompanied by increased excretion of fructose but lessened excretion of glucose or galactose. C. L.

SKVORTSOV (A.). Studies on the Life Cycle of *Dicrocoelium lanceatum*.—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian pp. 240–253. With 7 figs. [15 refs.] French summary p. 253.]

In the Moscow region Skvortsov investigated the development of *Dicrocoelium dendriticum* in the terrestrial mollusc *Helicella candidula*, and studied the morphology and bionomics of its egg. The shell consists of 4 membranes, the outer three permeable to water and salts, the inner impermeable to these but permitting the passage of organic compounds capable of dissolving fats and lipoids. The eggs remain viable at temperatures between +50°C. and –23°C. for 24 hours and are more resistant to desiccation than the eggs of *Fasciola hepatica*. On leaving the uterus the ovum of *Dicrocoelium* contains a fully

developed miracidium which hatches out in the "crop" of the vector. Thence it penetrates into its "liver," in the follicular connective tissue of which its transformation into sporocysts and cercariae takes place.

C. A. Hoare.

DIXON (H. B. F.) & SMITHERS (D. W.). **Epilepsy in Cysticercosis (*Taenia solium*).** A Study of Seventy-One Cases.—*Quarterly Jl. Med.* 1934. Oct. N.S. Vol. 3. No. 12. pp. 603–616. With 6 figs. on 3 plates.

Seventy-one cases of epileptic cysticercosis from the Queen Alexandra Military Hospital, Millbank, are described, 38 of them not having hitherto been published.

The frequency of this cause of epilepsy in patients from abroad is again stressed, as also its association with death of the parasite, its diagnosis by X-rays or by palpable cysts, the poor prospect of its treatment, and the lifting from the family of the fear of hereditary epilepsy.

C.L.

JOURNAL OF THE ROYAL ARMY MEDICAL CORPS. 1935. Feb. Vol. 64. No. 2. pp. 92–100. With 6 graphs.—**The Effect of Cooking on the *Cysticercus cellulosae*.**

"With the object of determining whether cooking, as ordinarily practised in the British Army, renders pork infested with the *Cysticercus cellulosae* safe for human consumption, a series of experiments was recently carried out in the Hygiene Department of the Royal Army Medical College."

The temperature reached in ordinary army cooking, with the exception of that of a burst sausage, was 65.5°C. a temperature which all authorities agree to be lethal for *C. cellulosae*. Baking, roasting and frying give the largest margin of safety since 75°C. is reached within the cooking time. Army cooking methods produce well done meat.

C. L.

MARTIN & ARNAUD; VELU (H.). **Epidémiologie de la "maladie hydatique" au Maroc.** Première Partie. L'échinococcose humaine [MARTIN & ARNAUD]. Deuxième Partie. L'échinococcose du bétail au Maroc [VELU]. [**Epidemiology of Hydatid Disease in Morocco.**—V. Congr. Ann. Féd. Sci. Méd. Algérie, Tunisie et Maroc (Oran 10–13 avr. 1935). 24 pp. With 1 map.

A statistical study of the incidence of hydatid in Morocco.

Here in the wet zones, where cattle are mostly raised, hydatid infection exists in cattle and sheep; in the south where there is little rain few cattle are raised. Judging by the presence of fertile cysts, sheep are less dangerous than cattle. In the former calcification is a part of cure, in the latter not so. It is not the number of hosts which is material, for a single dog—or perhaps, it is suggested as a point still needing settling, a single man—can infect many herbivora. The problem of the dog in rural areas is a hard one.

C. L.

BARNETT (Louis). **Formalin in Hydatid Cyst Operations.**—*New Zealand Med. Jl.* 1935. Feb. Vol. 34. No. 179. pp. 1–6. With 2 figs.

The need for the proper use of formolage in operating for hydatid cyst is stressed.

"Dévé and his collaborators have collected from the literature records of 133 cases of operative dissemination, and other noted authorities agree with him in estimating that this disappointing sequela occurs in from 3 to 4 per cent. of cases where formolage has been omitted. I have personal knowledge of at least half-a-dozen wound area recurrences occurring in the practice of colleagues and illustrative specimens can be seen in the Museum of the Otago Medical School."

The method of use of formalin is to expose the cyst and protect, by gauze wrung out in normal saline, the peritoneal cavity and all the wound surface from possible contact with escaping scolices. After evacuation of the cyst fluid by a Potain-type trochar, it is again completely filled with 2 per cent. formalin in water. After 5 minutes the cyst is incised and all parasitic material removed. Absolute contra-indications are cysts in or communicating with the lung and those in brain or cord, and the procedure is impracticable in cysts packed with daughter cysts.

C. L.

LEMAIRE & RIBÈRE. Sur la composition chimique du liquide hydatique.

[Chemical Composition of Hydatid Fluid.]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 15. pp. 1578-1579.

The chemical composition of hydatid fluid has been re-examined.

The mean figures are: S.G. 1.011.8; residue dried at 100°C. 13.72, ash 8.07, organic matter 5.65, chlorides (as NaCl) 5.96, urea 0.38, calcium 0.088, per litre in each case. Of cholesterol there was no trace in 27 per cent. of fluids, creatinin was constantly present with average of 9.5 mgm. per cent., inosite was present in 81 per cent. of fluids. A proteolytic ferment was always present thus explaining the absence of protein, when it is absent, and the inverse relationship here reported between albumin and amino acids; it acts best at a pH of 6.7, one which has been found present in hydatid fluid. There is also a glycolytic ferment. That is to say, creatinin, ammoniacal salts and lecithin are normally present in hydatid fluid and the existence of the ferments explains the different quantities of protein and sugar which have been reported.

C. L.

POISSON (H.). Note sur une localisation curieuse du *Cysticercus bovis*.

[Unusual Localization of *C. bovis*.]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 956-957.

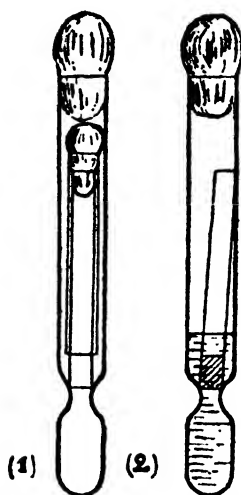
It is believed that in the calf *C. bovis* may occur in the liver, since a man who had been ordered raw liver passed a headless *Taenia saginata* and denied having eaten raw beef.

C. L.

LEMAIRE (G.) & RIBÈRE. Méthode simple et aseptique pour les essais de culture *in vitro* des scolex, applicable à l'étude des phénomènes biologiques susceptibles d'être observés de part et d'autre d'un ultra-filtre. [Culture of Scolices *In Vitro*.]—*C. R. Soc. Biol.* 1935. Vol. 118. No. 11. pp. 1080-1082. With 1 fig.

A method for keeping scolex-containing hydatid fluid sterile, and observing biological reactions.

As the figure shows there are 3 tubes originally sterilized. The outer is a Buchner tube which when sterile is filled to 2 or 3 cm. above the narrowing by serum, natural or artificial. The inner is of a diameter which will not pass the constriction in the Buchner's tube, and is

Culture of scolices in *vitro*.

(1) Apparatus used. (2) In operation.

[Reproduced from the *Comptes Rendus de la Société de Biologie*]

provided before use with an ultrafilter made by dipping its end into collodion solution and withdrawing it vertically so that a pellicle of collodion stretches across it and dries; if this is perfect, the ascent within the tube of the surrounding fluid is slow and in it are placed the sterile scolices, obtained with care for the maintenance of sterility. The middle tube is merely used to lift the inner one more readily in sterile conditions, the two being kept together by a tampon of cotton wool.

C. L.

SIEVERS (Olof). Serologische Untersuchungen ueber Bandwurm-antigene und ihre Antikörper. [**Serological Investigations of Tapeworm Antigens and Antibodies.**].—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Feb. 14. Vol. 84. No. 2/3. pp. 208–224. [Refs. in footnotes.]

The paper gives an account of experiments with antisera developed in rabbits by the injection of tapeworm antigen.

Alcoholic extracts of dried powdered substance of *Taenia saginata*, echinococcus and *Dibothriocephalus latus* were utilized, and also material which had been preserved in alcohol and then ground; various methods of preparing the injection material are described, one of which involves the use of pig serum as a vehicle. The antisera obtained were examined by the complement fixation and flocculation methods; the antigens were diluted by either a fractional or a rapid method but the dilution procedure caused no appreciable difference in results.

By quantitative experiments the author found evidence that a species-specific fraction is present in tapeworm substance.

Tests on patients harbouring *Dibothriocephalus latus* did not yield satisfactory evidence of the presence in their serum of tapeworm antibodies or antigen, but further experiments are contemplated.

D. B. Blacklock.

MILLER (Harry M.), Jr. **Transmission to Offspring of Immunity against Infection with a Metazoan (Cestode) Parasite.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 456-461.

"Offspring of female rats infected with *Cysticercus fasciolaris* showed a considerable degree of resistance to infection with onchospheres of *Taenia taeniaeformis*. Offspring of mothers actively immunized with *T. taeniaeformis* material had a lesser degree of resistance to infection with the onchospheres." C. L.

MILLER (Harry M.), Jr. **Experiments on Acquired Immunity to a Metazoan Parasite by Use of Non-Specific Worm Materials.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 27-34.

The definitive paper to which that already reported [this *Bulletin*, Vol. 29, p. 748] was preliminary. C. L.

ALTENKAMP (Th.). **Akute Appendizitis bei Bandwurm. [Acute Appendicitis in Tapeworm Infestation.]**—*Muench. Med. Woch.* 1935. Mar. 14. Vol. 82. No. 11. pp. 418-419.

In two appendices removed for appendicitis tapeworm segments were found. C. L.

PRÜMM (Albert). **Ueber hochgradige Eosinophilie bei *Taenia saginata*. [High Eosinophilia in *T. saginata* Infestation.]**—*Deut. Med. Woch.* 1935. Mar. 8. Vol. 61. No. 10. pp. 376-377.

An eosinophilia of 31 to 55 per cent. with no worm eggs in the stool, but with abdominal pain, remained unexplained until segments were passed. After removal of the worm eosinophilia rapidly disappeared. C. L.

GOLOB (Meyer). **Transduodenal Treatment of *Taenia saginata* Infestation.**—*Jl. Lab. & Clin. Med.* 1935. May. Vol. 20. No. 8. pp. 841-843.

An enthusiastic advocacy of the duodenal tube for treatment of *T. saginata* based on success with one case. C. L.

MAYEOZOKO (S.). **On the Distribution of *Hymenolepis nana* in Taito Prefecture, South-Eastern Part of Formosa, and its Mode of Infection.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1935. Apr. Vol. 34. No. 4 (361). [In Japanese pp. 459-470. [26 refs.] English summary p. 470.]

As the result of 7,618 faecal examinations, *H. nana* was found in 28.6 per cent. between 2 and 5 years old, in 44.6 per cent. between 6 and 10, in 10.7 per cent. between 10 and 15, and was very rare over 16 years. C. L.

LAPAGE (Geoffrey). **The Bearing of the Physiology of Parasitic Nematodes on their Treatment and Control.**—21 pp. [16 refs.] 1935. Imperial Bureau of Agricultural Parasitology. Winches Farm Drive, Hatfield Road, St. Albans. [3s.]

The gaps in knowledge of the physiology of parasitic nematodes are such as almost entirely to prevent advance in their control.

The aim of control is put thus:—

"Our task . . . should not be the impossible one of attempting to rid human beings or farm animals of all their nematode parasites,

or of trying to keep them free from these, but the very difficult but at least possible one of keeping these infections within bounds."

Indeed it is suggested that worm-free animals may possibly not be as healthy as those with a worm load since "the latter have evolved in association with these parasites and therefore are adapted to their presence," so that it is wiser "to seek to produce animals healthy because they are in equilibrium with their parasites" than to deworm. It is urged that knowledge of the physiology and so of the control of parasites will be incomplete until they can be kept alive in all stages *in vitro*. The unsheathing of larvae as a means for their destruction is considered. It is held unproved that blood imbibed by worms is used as food [haemoglobin is certainly absorbed]. Remedial measures based on a knowledge of the physiological relationship existing between host and parasite "would relieve us, for example, from the use of carbon tetrachloride which, efficient though it is, may have effects on the host, even when it is used by experienced workers, which are worse than those of the disease which it is designed to cure." C. L.

TUBANGUI (Marcos A.), BASACA (Mariano) & PASCO (Antonio M.).
Human Infestations with Ascaris and Trichuris in Different Parts of the Philippine Islands.—*Philippine Jl. Sci.* 1934. Oct. Vol. 55. No. 2. pp. 91–113. With 4 figs. [16 refs.]

A study by Stoll egg counts of ascaris and trichuris infection in 3 places in the Philippine Islands.

The percentages of infection and the estimated number of eggs per cc. were: for ascaris 79.5 and 16,800, 74.3 and 15,800, 84.5 and 28,870; and for trichuris 88.1 and 4,400, 58.1 and 890, 87.3 and 2,900. Children are more often and, judging by egg counts, more heavily infected than adults. Ascaris infection was associated with soil fouling about houses, mainly produced by children of pre-school age.

C. L.

LAMSON (Paul D.), MOLLOY (Daniel M.) & BROWN (Harold W.).
Field Studies of the Anthelmintic Action of Ortho-Heptylphenol and 6-Hexyl-Meta-Cresol against Ascaris lumbricoides, Necator americanus and Trichuris trichiura.—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 188–199.

The authors report as follows:—

"1. Ortho-heptylphenol and 6-hexyl-meta-cresol, substances which are the lowest members of their respective series of ortho-alkylphenols and 6-alkyl-meta-cresols which cause no whitening of the oral mucous membranes, have each been tested for their anthelmintic properties in approximately 100 cases harboring *Ascaris*, *Necator*, and *Trichuris*.

"2. Ortho-heptylphenol reduced the egg count in ascariasis approximately 35 per cent., in uncinariasis, 60 per cent., and in trichuriasis, 40 per cent., in doses as great as 4 cc.

"3. 6-hexyl-meta-cresol reduced the egg count in ascariasis approximately 55 per cent., in uncinariasis, 70 per cent., and in trichuriasis, 30 per cent., in doses as great as 4 cc.

"4. In the 220 cases treated, no pathological signs or symptoms were noticed, no complaints were made by the patients, and all went about their daily work without interruption.

" 5. It is of interest to note that these two phenols have a relatively greater action on *Necator* than on *Ascaris*, as is the case with thymol, but which is the reverse of the action found in the alkyl resorcinols, as hexyl- and heptylresorcinol."

The method of egg counting was by 2 slides using the Stoll-Hausheer technique, or 0.01 cc. of faeces in all. C. L.

ADAMS (A. R. D.). **Ascariasis of the Liver.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 419–420.

An acute abdomen with ruptured hepatic duct killed a Mauritian creole, 73 years old.

Autopsy showed one ascaris in the hepatic duct, seven in the bile-free gall bladder, and 10 in the bile passages of the right lobe of the liver. All were adult. The bile ducts exuded yellow muco-pus with many fertile and unfertile ascaris eggs, but though there was a mild subacute cholangitis there was no abscess formation. It was not possible to obtain the entire intestine for examination. C. L.

ALBERT (Jose) & PAULINO (Peregrino). **Mimicry in Ascariasis.**—*Jl. Philippine Islands Med. Assoc.* 1934. Dec. Vol. 14. No. 12. pp. 463–469.

Of 8 patients, one had symptoms simulating meningitis, one had melaena, one profuse haematemesis, one acute toxæmia, one severe abdominal pain, two abdominal tumours disappearing with anthelmintic treatment, one acute bronchopneumonia, and one ileocolitis. C. L.

MU (Jui-Wu). **Local Skin Reactivity in Rabbits to an Extract of *Ascaris lumbricoides*.**—*Proc. Soc. Experim. Biol. & Med.* 1935. Apr. Vol. 32. No. 7. pp. 995–997.

Author's summary :—

" Intradermal injection of rabbits with an extract of *Ascaris lumbricoides*, followed 24 hours later by intravenous administration of the same extract, produced hemorrhagic necrosis which grossly and microscopically conformed with that described by Shwartzman." C. L.

KAMIMURA (Takeichi). **Report of a Case of Pulmonary Abscess caused by the Migration of an Adult *Ascaris* in Bronchi with a Review of Literature on the Injuries caused by *Ascaris lumbricoides*.**—*Jl. Oriental Med.* 1935. Apr. Vol. 22. No. 4. [In Japanese. English summary p. 62.]

After a death from rabies an ascaris was found in bronchi of the upper and lower lobes of the right lung and the lobes themselves contained abscesses. The summary does not refer to the literature reviewed. C. L.

GIRGES (Rameses). **II.—Diagnosis of Ascariasis.**—*Jl. Trop. Med. & Hyg.* 1935. Mar. 1. Vol. 38. No. 5. pp. 55–59. With 1 fig.

Largely a summary of literature in whose compiling the author acknowledges his indebtedness to this *Bulletin*. C. L.

- FÜLLEBORN (F.), DIOS (Roberto L.) & ZUCCARINI (Juan A.). Bericht ueber eine im Auftrage der argentinischen Regierung unternommene Reise nach der Provinz Corrientes und nach Paraguay zum Studium der Hakenwurmbekämpfung mit Bemerkungen zur Frage der Immunität gegenüber Hakenwürmern.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1928. Vol. 32. No. 9. pp. 441–481. With 6 figs. (1 map). [58 refs.]
- , — & —. Estudio acerca de la anquilostomosis en la provincia de Corrientes (encomendado por el Gobierno Argentino). [*Ankylostomiasis in the Province of Corrientes, Argentina.*]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. July. Vol. 6. No. 3. pp. 249–294. With 5 figs. & 1 map. [58 refs.]

A belated abstract of work done in the Argentine before 1928 and recently republished.

Corrientes lies to the south of Paraguay and west of Rio Grande. The authors examined 396 of the civil population of ages ranging from 3 to over 60 years. They estimated the relative proportions of *Necator* and *Ancylostoma*, the clinical effects of infestation, the existence of helminths other than hookworms and they devote a section to prophylaxis. The reader must judge of the degree of the reliance he can place on findings based on so small a number of examinations; the authors state that in the northern part of the Province practically 100 per cent. of the rural population are infested with hookworms and fairly heavily. In children from 3–10 years there were on an average 4,816 ova per gram of (pasty) faeces (approximately 390 worms); in those from 11–20 years 6,885 ova (= 550 worms); from 20 years up 2,152 or 170 worms. In all districts visited infestation was greater in the young and in the females at all ages. Among soldiers who had been 3–4 months in barracks the degree of infestation was about half that of the civil population of the same age in the north of the Province, and 93–94 per cent. of the worms were *Necator*. Blood disturbance was comparatively slight; even in those heavily infected the Hb percentage was about 81 in men and 74–75 in women. The resistance to the results of infestation is ascribed to the diet containing plenty of meat and to the fact that there is considerable crossing with Indian blood. Of other worms *Trichuris*, *Ascaris* and *Strongyloides* were not uncommon and *T. saginata*, *H. nana* and *Enterobius* were also met with. Nothing fresh is suggested regarding prophylaxis.

H. H. S.

- JAMAICA. ANNUAL REPORT OF THE MEDICAL DEPARTMENT FOR THE YEAR ENDED 31st DECEMBER, 1933 [HALLINAN (T. J.), Supt. Med. Officer].—102 pp. With 1 chart & 5 maps. 1934. Kingston. [*The Jamaica Hookworm Commission.* Appendix I, pp. 61–62.]

The work of the Jamaica Hookworm Commission, the direct descendant of the Rockefeller Hookworm Commission of 1919, is described for 1933.

In any area to be dealt with there are first made pit latrines at least 8 feet deep, with sloping sides to prevent collapse, and if in sandy soil lined with flat stones. The top is surrounded by a cement wall, high enough to prevent splashing if the ground water is high, and on this is placed a fly-tight seat box made of sound wood. Only in a demonstration area so prepared is treatment instituted. A trained inspector has charge of each area carrying 300 to 500 persons. After

explanation of reasons for the whole procedure faecal specimens from all persons are obtained (in 1933 from 38,698 of a total population of 38,745) and examined by Willis's direct gravity floatation method. The percentage found infected was 74. Treatment was given to 25,183, of whom 83 per cent. were held cured. The adult treatment was 24 minims of oil of chenopodium of unstated ascaridole content, a week later 40 grains of thymol, and a week later still, another faecal examination. C. L.

YACOB (M.) & CHAUDHRI (J. R.). **Hookworm Infection in the Punjab. Survey of a Rural Area in Ambala District.**—*Indian Med. Gaz.* 1934. Dec. Vol. 69. No. 12. pp. 669–672.

The results of a hookworm survey of 2 villages near Ambala, Punjab, India.

Stools of 150 persons were examined by a modified D.C.F., and egg counts were made on 100 of them by a modified Stoll's method. The incidence percentage was 82 and the average eggs per gram 422.7. The faeces had been transmitted by Maplestone's method. Of 119 persons found infected, 15 are classed as normal with no clinical symptoms and 192.5 eggs per gram, and the authors note "the fact that, on an average, an egg count of 192.5 is not of any clinical significance" [their average haemoglobin was 57.7]; 47 were moderately incommoded, usually by anaemia with or without digestive disturbance, and with an average egg count of 356.3 [their average haemoglobin was 56.9]; and 57 were severe cases with marked anaemia, breathlessness and palpitation and with an average egg count of 586.1 [their average haemoglobin was 52.1]. The incidence of infection was highest among cultivators, lowest among shopkeepers, with labourers and artisans intermediately placed, higher in males than in females, and higher in those below 40 years of age than in those above. House latrines are few, the sides of footpaths being mainly used. Women and children go barefoot; such males as do not nevertheless work barefoot in the fields. The modification of D.C.F. was that

"The cover-slips, instead of being placed on plasticine cones, were placed directly on a microscopic slide and examined in the usual manner under the microscope. We found this modification of Lane's technique much more expeditious and convenient to work with than the original technique."

[The modification implies the need to examine about 400 sq. mm. instead of 9 sq. mm., while refraction of light at the edge of the cover renders invisible any eggs which may lie near it.] C. L.

BERTINI (Gennaro). **L'anchilostomiasi nella provincia di Firenze dal 1925 al 1930.** [**Ankylostomiasis in the Province of Florence, 1925–30.**]—*Ann. d'Igiene.* 1935. Jan. Vol. 45. No. 1. pp. 32–40.

Ankylostomiasis, due to *A. duodenale*, is widespread in Italy and endemic in the Province and Commune of Florence. Some 400 cases have been found in 4 or 5 years. Fifty "infested zones" are mentioned with a total of 372 cases, but in 9 of the "zones" there was only a single case each, and 38 have under ten. The populations of these zones are not stated, so the incidence rate cannot be given. Of the total, 134 or 36 per cent. were between 10 and 20 years of age

and another 111 between 20 and 30 years ; 179 were males and 193 females, all peasants or gardeners working in soil kept moist by irrigation. "Diagnosis appears to have been made by direct smear.]

H. H. S.

MALDONADO SAMPEDRO (Mariano). Un foco de necatoriasis importado. en Castañar de Ibor. [**A Focus of Imported Hookworm Cases in Castañar de Ibor.**—*Medicina Paises Cálidos*. Madrid. 1935. May. Vol. 8. No. 5. pp. 217-232. With 4 figs. [35 refs.]

Examination of a family, which had returned to this locality in Spain three years previously after living for a time in Brazil, revealed the presence of hookworm in the mother. Further enquiry and examination of three other families comprising 25 individuals resulted in the discovery of 21 more passing the ova of *Necator*. Most of them were children. These three families had also returned to the district from abroad. Castañar de Ibor is north of the Sierras de Guadalupe separating Cáceres from Toledo. Now that the presence of these carriers is known steps will doubtless be taken to prevent infestation of other residents.

H. H. S.

WICKRAMASURIYA (G. A. W.). **The Grave Risks of Hook-Worm Disease as a Complication of Pregnancy.**—*Jl. Obstet. & Gynaecol. Brit. Empire*. 1935. Apr. Vol. 42. No. 2. pp. 217-267. With 7 figs. (4 on 2 plates). [18 refs.]

At the De Soysa Lying-in Home in Colombo with total admissions of 5,500 a year, the highest death rate for both mother and child was due to hookworm infection.

Of 273 deaths which occurred in 1932-33, hookworm infection accounted for 27 per cent., puerperal sepsis for 12·8. Of 100 consecutive still-births 23 were due to hookworm infection, 14 to breech presentation, and 11 each to syphilis and pre-eclampsia ; but this does not represent the hookworm's real effect on keeping down the live birth rate, since it takes no count of the abortion and miscarriage which the infection commonly causes. About 90 per cent. of those with hookworm disease show albuminuria and oedema in the last half of pregnancy. The pains of labour are often absent, perhaps from the mental dullness often present. The puerperium is often complicated. There may be fatal heart failure in labour or the puerperium, or the cardiac reserve may be permanently impaired. After delivery the anaemia may rapidly improve [the foetal hunger for iron has gone] but cardiac and renal reserves may never fully recover.

In the common oedematous clinical type the blood urea in mgm. per cent. is raised from local minima, average and maxima of 9, 15·25 and 20 (in 11 healthy cases) to 21, 57·3 and 73·5 (in 37 with hookworm disease) and renal function is always lessened from corresponding figures (in 10 cases) of 2·8, 3·3 and 4·0 to 1·3, 1·7 and 3·0 (in 37 cases), the urine being scanty, with low specific gravity and containing albumin and casts ; in the 7 case histories given, haemoglobin varied from 15 to 35. In the rarer non-oedematous type the blood urea is usually below 20, albumin at most a trace, casts absent. When haemoglobin (which may be as low as 15) falls to 40 renal function becomes defective, urea concentration perhaps falling below 2 per cent. The diagnosis from pre-eclampsia, chronic nephritis, and pernicious anaemia of pregnancy is dealt with. Prognosis of that weight of

infection which the author has in mind is grave for both mother and child. As to the mothers 9 died during pregnancy, 7 during labour and 58 in the puerperium, and of these last the causes of death were cardiac failure 40, post-partum shock following normal delivery 7, sepsis 5, dysentery 3, pyelitis 2, and malaria 1, so that concomitant illness is a large feature in causing death. C. L.

CRUZ (W. O.) [In Portuguese & English]. Pathogenia da anemia na ancylostomose. II.—Causas determinantes dos phenomenos regenerativos e degenerativos nessa anemia e contribuições para elucidar o seu mecanismo intimo. **Pathogenesis of Anaemia in Hookworm Disease. II.—Causes which determine the Regenerative and Degenerative Phenomena in this Anaemia and Contributions towards the Elucidation of their Inmost Mechanism.** III.—Modificações hemáticas e orgánicas, provocadas pelas simples eliminação do Ancylostomo e do Necator, em individuos fortemente anemiados. **III.—Hematic and Organic Modifications, induced by Mere Elimination of Ancylostoma and Necator, in Individuals presenting Intense Anaemia.**—*Mem. Inst. Oswaldo Cruz.* 1934. Vol. 29. No. 2. In Portuguese pp. 263–426. With 30 graphs. [104 refs.]. In English pp. 427–485; In Portuguese pp. 487–540. With 10 graphs. [23 refs.] In English pp. 541–561.

The English version is not easy to understand, but it is believed that these notes render it rightly.

II. In 25 cases of ankylostomiasis it is confirmed that the anaemia is hypochromic and microcytic with little evidence of regeneration. The red cells lay between 900,000 and 4,580,000, their haemoglobin between 10 and 40 and their volume between 6 and 25. The presence of normoblasts, nuclear remainders and polychromatism was very rare. Iron is the only substance of value in treatment; raw liver, tryptophan, histidine, vitamin B, cobalt, manganese, arsenic, copper and diets rich in iron were useless. Iron eliminates degenerate red cells and causes reticulocytes to be made with an initial macrocytosis. It is held that with this treatment blood always becomes completely normal. Actually, the minimum average and maximum figures recorded at the end of treatment were: red cells in millions 3.55, 4.53 and 5.25, haemoglobin 62, 77 and 91, haemocrit readings 27, 33.7 and 41. As anaemia improves symptoms disappear. All these good effects are seen while the worms are left.

"During the observation of the course of the anemia, the degeneration of the hematic indices becomes conspicuous as an important factor both in the hypofunction of blood and in occasioning the appearance of the symptoms of the disease. We verified that, with one and the same Hb. rate in the circulating blood, the symptoms may either appear with great intensity or be absent according as the hematic indices may be degenerated or normal."

Accordingly it is held that the anaemia is not the result of a toxin nor of haemorrhage but is due to disturbance of iron metabolism.

III. Ten cases of ankylostomiasis were given anthelmintic but no other treatment. The minimum, average and maximum figures were: red cells before treatment 2,070,000, 2,620,000, 3,530,000 and after anthelmintic treatment 2,370,000, 4,270,000, 5,620,000; haemoglobin before treatment 22, 27.5, 38, and after it 23, 47.5, 75. The final conclusion is this:—

"The absence of blood modifications ascribable to elimination of the intestinal parasites and the resemblance of the blood regenerations induced

by iron both in the presence of helminthes in the intestine and after previous elimination of these parasites are very important verifications for the elucidation of the pathogenesis of the disease, and tend to confirm the essential importance of an organic insufficiency (iron deficiency) in the determination of the anemic syndrome and of the disease." C. L.

LANDSBERG (J. W.) & CROSS (S. X.). **The Blood Picture in Acute Fatal Infestations with *Ancylostoma caninum*.**—*Jl. Parasitology*. 1935. Apr. Vol. 21. No. 2. pp. 130-132. With 1 fig.

The infection produced an acute post-haemorrhagic anaemia, with a blood loss so great that death was inevitable, the haemopoietic system being unable to keep pace with the drain.

The puppies, 2 months old, were given by mouth "lethal doses" of hookworm larvae in gelatin capsules and died within 17 days of infection.

Besides the changes in erythrocytes shown in the accompanying table there was anisocytosis, slight poikilocytosis and achromia. The mucous membranes at death were perfectly white. No mention is made of any faecal blood passed during life or of blood in the intestinal contents after death.

Showing changes in the red cell picture during course of infection of three dogs (litter mates) with A. caninum.

Days on experiment	D 876			D 877			D 878		
	R.B.C.	Hb. (gm.)	C.V.	R.B.C.	Hb. (gm.)	C.V.	R.B.C.	Hb. (gm.)	C.V.
1	5.01	8.4	74	5.12	7.4	78	4.09	6.4	61
3	5.04	7.6	75	4.91	8.0	78	4.51	6.9	69
13	5.00	8.7	77	5.29	9.9	69	5.69	8.9	69
13		Infected			Infected			Infected	
17	4.77	6.7	63	4.78	6.7	63	4.62	6.7	63
20	4.95	6.7	69	4.89	7.6	74	5.09	7.3	75
24	3.03	4.5	67	3.87	5.5	75	4.46	6.4	67
27	1.93	2.7	68	3.06	4.3	65	3.97	5.0	72
29	1.61	2.1	62*					4.6	
30				2.16	2.2	65*	2.99	4.3	65*

R.B.C. = the number of red blood cells per cmm. blood expressed in decimals of a million (5.01 = 5,010,000).

Hb. = grams of hemoglobin per 100 cc. blood.

C.V. = the mean corpuscular volume in cubic microns.

* Blood sample obtained from heart immediately following death.

C. L.

FOSTER (A. O.) & CORT (W. W.). **Further Studies on the Effect of a Generally Deficient Diet upon the Resistance of Dogs to Hookworm Infestation.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 302-318. With 3 graphs.

"Experimental studies on twelve dogs have furnished additional evidence that a generally deficient diet renders them more susceptible to infection with *Ancylostoma caninum*."

"Seven of these animals which were kept until death on the deficient diet, showed a terminal breakdown of resistance which was characterized by a sharp increase in the daily egg productions of the infestations during the last 2 weeks of life. At autopsy these animals were found to be heavily parasitized, the number of worms varying from 155 to 614 in dogs which were from 7 to 19 months old at the start of the experiments. The data indicate, in general, that the resistance of the younger animals was more easily broken down by the deficient diet."

C. L.

MAPLESTONE (P. A.). **A Simple Method of growing Hookworm Larvae.**—*Indian J. Med. Res.* 1934. Oct. Vol. 22. No. 2. pp. 203–214. With 1 text fig. & 2 figs. on 1 plate.

Maplestone describes and illustrates the apparatus with which he made his previous cultural experiments on hookworm eggs; he reports that larvae will not migrate from culture apparatus of this type and that it is necessary to extract cultures for at least 2 successive days to be sure that nearly all the larvae they contain have been extracted.

These particular experiments were entirely uncontrolled generally or individually "because it has been shown by Maplestone (1924) [this *Bulletin*, Vol. 21, p. 967] that this is an efficient method of growing hookworm larvae, for it was used on that occasion to check the value of Stoll's egg-counting method, and many times more larvae were extracted from cultures than one was led to expect from the number of eggs estimated by counting." A piece of gauze made of non-corrosive wire, with 1 mm. mesh and 12 cm. square is, by overlapping the corners, made into a square basket with bottom 6 cm. long and sides 3 cm. deep the addition to which of a wire loop makes handling safer and quicker. In the basket is first put a covering of 50 cc. of coarse sand or small glass beads and then in a hollow made in this 8 cc. of earth which has been put through 3 mm. mesh gauze after being heated to 70°C. while moist and then pounded in a mortar. On the earth is poured 4.4 cc. of broken up faeces and water unmeasured but of the same degree of seeming fluidity. The baskets rest by their corners in inverted truncated cones of aluminium open at both ends, and these in turn in petri dishes containing a little water. The corners of the baskets are about 4.5 cm. from the surface of the water. The whole is put under a bell jar. No larvae were ever found in the water in the Petri dish, nor were they in closed funnels when the water in these was within 2 or 3 mm. of the bottom of the basket. But experiments made by suspending small baskets 3 cm. square on rods which rested on the mouths of beakers showed some larvae below them. [Presumably they got there either by forming the threads familiar in FÜLLEBORN's experiments, or by climbing up the suspending wire along the rod to the edge of the beaker and down the wall of the beaker to the water.] Extraction from these cultures disclosed from 277 to 982 larvae, but has to be continued for 2 days to show up most of them, 5 per cent. more being accounted for by continuing extraction for 7 days.

Maplestone thus quotes and contradicts the reviewer's view of the "unescapable need to trap cultures."

[This quotation divorced from its purpose and context is misleading. LANE, 1928, begins "Under grants from the Royal Society the writer has, during the past 2 years, been endeavouring to disentangle the

various factors which determine whether hookworm ova shall develop into larvae and whether larvae shall grow to infectivity." And LANE, 1932, in its first sentence says—"I have tried to separate the factors which favour their [hookworms'] extracorporeal development." To do so two things were necessary: to know the number of eggs with which each experiment started, and to be sure that all larvae that matured were accounted for. Maplestone has not attempted the first; as to the second the conditions do not seem to preclude a great likelihood of the death of larvae in their attempt to leave the cage.]

C. L.

WATSON (W. H.). **Drainage as a Controlling Factor in the Spread of Hookworm.**—*East African Med. Jl.* 1935. Jan. Vol. 11. No. 10. pp. 308-315. With 9 figs. [14 refs.]

The author in Nyasaland reaches the following conclusions:—

"It is considered that the [natural] drainage factor plays a most important part in controlling the incidence of hookworm infestation among the native population of plain districts such as Port Herald [in which it is high] as compared with the population of mountainous districts such as Zomba [in which it is low]."

C. L.

LANE (Clayton). **The Appraisal of Hookworm-killing Drugs.**—*Lancet.* 1935. June 22. pp. 1459-1464. [40 refs.]

The author points out that accurate scientific determination of the actual vermucidal value of any drug, and consequently the relative values of several cannot be reached unless answers are first obtained to certain questions, namely: 1. Should deworming be complete? 2. Do egg-counts measure worm-loads? 3. Do egg-counts measure faecal egg-content? 4. Which is the best diagnostic technique?

The evidence *pro* and *contra* for each of these is impartially marshalled. Colonel Lane shows as regards the first that a few (7-8) hookworms may give rise to severe symptoms while in another patient more than ten times as many may not. Hence, in the interest of the host, complete deworming should be the aim of treatment. As regards the second the author has himself shown that worm loads cannot be measured by faecal egg-counts with any approach to accuracy. Whether egg-counts are a measure of faecal egg-content depends obviously on the accuracy of the method employed, and putting natural bias aside (not an easy thing to do) the author shows by evidence that the D.C.F.F. technique is not only the most accurate egg-counting method, but that by it the faecal egg-content can be measured more accurately than by any other, provided the directions for its use are followed in every particular [this is a point which does, though it ought not to, need stressing].* The fourth question is thus inseparable from the third and the same answer applies. To sum up: "Evidence for complete deworming is the only stable criterion of drug efficiency" and "hygienic risk caused by infected persons can be graded rapidly, usefully and empirically" by the D.C.F. technique. Also "the lessening of hygienic risk produced by mass treatment is the proper and adequate measure of the success of such treatment."

* "D.C.F. or direct centrifugal floatation is a qualitative (yes or no) diagnostic technique which examines a single specimen obtained by a single centrifuging. D.C.F.F. or direct centrifugal floatation pushed to finality, is a quantitative technique, aiming at disclosing the total number of eggs present by examining 4 (plus 1) specimens from 4 (plus 1) centrifugings."

The following drugs are next considered *serialim*: Oil of chenopodium, thymol, carbon tetrachloride, tetrachlorethylene and hexyl-resorcinol. Oil of chenopodium has no stable composition; its active principle, ascaridole, is very variable between 33 and 98 per cent. Though it is given arbitrarily regardless of the ascaridole content such a procedure is indefensible. Many tens of thousands of doses have been given and results of a kind reported, but only in a small proportion has the amount of active principle contained been known and the measurement of success has been gauged by other means than proof of deworming; hence, as the author states, he finds "no acceptable published evidence of its efficiency against hookworms."

Thymol crystals readily agglomerate into a mass and for success this drug must be particulated as, for example, by mixing with an adequate quantity of sugar of milk. It is, or has been, often taught that absorption should be prevented, but Lane holds that the drug only acts after absorption. Evidence goes to show that two, 60 grain, courses of the drug will result in deworming in about half the cases in adults. It is a safe drug in practice because toxic symptoms occur early and the intoxicating dose is well below the lethal dose.

As regards carbon tetrachloride, it has been stated that after large doses much is passed unchanged and that large doses are safer than small ones. This is hardly credible, for the amount absorbed constitutes the danger. The minimum lethal dose is 1.5 cc. but doses up to double this are often given and its toxic effects depend on individual susceptibility.

The dosage of tetrachlorethylene employed by GARRISON is 3 cc. weekly, 1 cc. in three successive hours, for a child of 10 years, the patient being kept in bed on the day of treatment and the third dose being followed by a purge. This quantity is given for 3 weeks, *i.e.*, 9 cc. in all. No death has as yet been reported and "the drug merits massive, controlled, field investigations, but present claims to its pre-eminence are premature."

No attempts have been made to evaluate the results of hexyl-resorcinol by the only sound test—deworming. It is liable to cause local irritation and erosion and on that account its purchase has been restricted in U.S.A.

In default of deworming tests there remain comparative tests with control of single factors. One such (the only one discoverable) was effects of thymol in a 60 grain dose, ascaridole 1 cc., and carbon tetrachloride 1 cc. on *A. duodenale* and *N. americanus*, by CAIUS and MHASKAR using the Schüffner-Vervoort method. Thymol gave 96.1 and 99.6 per cent. success on the two worms respectively, ascaridole 60.9 and 83.4, and carbon tetrachloride 11.5 and 90.8. This supports the author's conclusion that thymol heads the list "especially when safety and efficiency are both considered, it being again stated emphatically that *safety must have the first place*." [The article, apart from its intrinsic value, has the additional merit of almost necessarily provoking argument and further research.] H. H. S.

- i. TUXFORD (A. S.); ii. LANE (Clayton). **Administration of Carbon Tetrachloride for Hookworm.** [Correspondence.]—*Lancet*. 1935. June 1 & 8. pp. 1302; 1357.

- i. Tuxford advocates carbon tetrachloride with castor oil for hookworm. Having treated many hundreds of such cases without a death

he advises 3 cc. of tetraform with $\frac{1}{4}$ oz. of castor oil. Discomfort after it is rare. It is advised as having no ill effects.

ii. Lane points out that GIGLIOLI [this *Bulletin*, Vol. 21, p. 972] felt that the same result was produced by shaking carbon tetrachloride in water, and that both experiments were uncontrolled and of insufficient extent. The only animal experiment traced was one by Maurice HALL; it suggested that the mixture was not efficient; but this could not be determined by herd treatment. C. L.

VAN SLYPE (W.). Sur la détermination des strongylides humains d'après les dimensions de leurs oeufs. [**Determination of Human Strongylidae from Dimensions of Ova.**]—*Bull. Soc. Path. Exot.* 1934. Dec. 12. Vol. 27. No. 10. pp. 939-942.

The range of the paper is that which the title shows.

The paper concerns Lomami, in Katanga, and judging by the size of the eggs, presumably in smears, of 100 persons examined the percentages infected with the various strongyle parasites were estimated as follows: *A. duodenale* 53, *N. americanus* 74, *A. braziliense* 2, *Ternidens* 19, *Trichostrongylus* 10. Of the *ternidens* egg the distinctive points are its width of 45-56 μ , its length of 73-80 μ , its double contour, the cells numbering 6 to 12, well defined with obvious refractile nuclei, the shell having a double contour. C. L.

MCCOY (O. R.). **Artificial Immunization of Rats against *Trichinella spiralis*.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 200-213.

The author's summary is as follows :—

"The majority of rats given six intraperitoneal injections at 5-day intervals of living trichina larvae, heat-killed larvae, or dried and powdered larvae, developed some degree of immunity against a subsequent light infection with *Trichinella spiralis*. The degree of immunity in the individual animals varied from none to practically complete. The injection of living larvae was usually more effective in establishing immunity than the injection of either heat-killed larvae or dried and powdered larvae. Artificially immunized rats showed little or no resistance to the initial development of adult worms in the intestine but the worms were lost more rapidly than in control animals. This, of course, would result in a smaller amount of muscle invasion in the immunized rats. The immune state produced by the injections is apparently of the same general nature as that brought about by actual infection; in each instance the mechanism is directed against the intestinal stages of the parasite. The former immunity, however, is not nearly as potent as the latter and is much more easily broken down by large doses of larvae." C. L.

ROTH (Hans). Ein Beitrag zur Frage der prenatalen Trichineninfektion. [**Prenatal *Trichinella* Infection.**]—*Acta Path. et Microb. Scandinavica.* 1935. Vol. 12. No. 1-2. pp. 203-215. [25 refs.]

Foetal trichinous infection was produced in guineapigs, the larvae in the young being at the same stage of their development as those in the mothers. C. L.

BAUDET (E. A. R. F.). Over de werking van causyth op trichinen bij ratten. [Action of Causyth on Trichinae in Rats.]—*Tijdschr. v. Diergeneesk.* 1935. May 15. Vol. 62. No. 10. pp. 527-532. English summary (6 lines).

Causyth, a coal-tar preparation containing sulphur, was used with apparent success by WELTMANN (1931) in a case of human trichinosis. The author found it useless in the prevention of intestinal or muscular trichinosis in rats, and concludes that its action in man was not specific.

A. G. B.

WU (L. C.). Chronic Salpingitis caused by *Oxyuris vermicularis*. Report of a Case.—*Chinese Med. Jl.* 1935. Mar. Vol. 49. No. 3. pp. 256-259. With 2 figs. on 1 plate.

A small yellowish nodule in the wall of the left fallopian tube showed on section many thread worm ova in a "capsule." The faeces showed ascaris ova. The operation had disclosed much-dilated, tortuous and congested tubes matted to ovaries and uterus.

C. L.

SCHULTZ (R.) & IVANITSKI (S.). Gongylonematosis of Man, with the Description of a New Case.—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 6. [In Russian pp. 516-527.]

The total number of cases of Gongylonema infections reported from man is seven. The authors describe a new case from Kharkov (Ukraine). A review is given of the literature on gongylonematosis and the question of its possible rôle in the aetiology of cancer is discussed. The parasite is identified as *Gongylonema pulchrum*.

C. A. Hoare.

KELLER (Alvin E.). The Occurrence of Eggs of *Heterodera radiculicola* in Human Feces.—*Jl. Lab. & Clin. Med.* 1935. Jan. Vol. 20. No. 4. pp. 390-392. With 1 fig.

The eggs were obtained from the faeces of 34 of 44,380 whites and 5 of 6,441 negroes in Mississippi. It is believed that they can be mistaken for unfertile ascaris or hookworm eggs and so may lead to unnecessary giving of anthelmintics.

C. L.

HU (Stephen M. K.) & YEN (C. H.). Studies on the Comparative Susceptibility of *Culex pipiens* var. *pallens* Coquillett and *Culex fatigans* Wiedemann to Experimental Infection with *Wuchereria bancrofti* Cobbold.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 483-490. [12 refs.]

A continuation of experiments already recorded [this *Bulletin*, Vol. 31, p. 804] on susceptibility of the mosquitoes noted in the title.

The maximum microfilarial count in the mosquito-meal-provider was 248 in 20 cmm. of blood as compared with 23 in the earlier series. Both species of *Culex* were fed on him at the same time and the time of reaching full development in each was about the same, and of those surviving for this period 90.1 per cent. of *C. p. pallens* and 94.5 per cent. of *C. fatigans* were infective. In both, larvae from one feed might fail to reach infectivity while those from another might do so. The average number of infective larvae in each *C. p. pallens* was 14.4 and in each *C. fatigans* 7.3.

C. L.

HU (Stephen M. K.). **Experimental Infection of *Culex fatigans* Wiedemann from Foochow, Fukien Province, with *Wuchereria bancrofti* Cobbold.**—Reprinted from *Lingnan Sci. Jl.* Canton. 1935. Jan. 1. Vol. 14. No. 1. pp. 87–92. [10 refs.]

Of 193 *Culex fatigans*, bred from larvae collected in Foochow and fed on a filarial subject with many microfilariae in the blood, 70 per cent. harboured embryos on dissection; 141 survived the period of incubation and of these 96 harboured infective larvae, that is 50 per cent. of those fed and 68 per cent. of those surviving. C. L.

FENG (Lan-chou). **Some Experiments with Mosquitoes and *Microfilaria malayi* in Huchow (Chekiang, China).**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 491–494.

The author gives the following account of his experiments.

"1. Experiments with five species of mosquitoes for the transmission of *Microfilaria malayi* were carried out in Huchow, Chekiang Province in the summer (July–August) of 1933.

"2. Partial development of *Microfilaria malayi* took place in *Culex pipiens*, *Stegomyia albopictus* and *Armigeres obturbans*.

"3. Normal development of *Microfilaria malayi* has been observed in *Mansonia* (*Mansonioides*) *uniformis* up to the 4th day after which a certain number of the embryos died and only comparatively few reached maturity 8 days after the infective feed.

"4. Normal development of *Microfilaria malayi* took place in *A. hyrcanus* var. *sinensis*. The filarial embryos reached maturity on the 6th day and from the 6th to the 8th day after the infective feed invasion of the labium by mature larvae was very common. As many as 59 mature, actively motile larvae have been found in one mosquito in various parts of the body including the labium.

"5. *A. hyrcanus* var. *sinensis* is probably the most important carrier of *Microfilaria malayi* in the Huchow area although *Mansonia* (*Mansonioides*) *uniformis* may also participate in the transmission of this parasite." C. L.

ROMITI (Cesare). **Filariasis in British Guiana. A Comparative Study of *Filaria bancrofti* and *Filaria ozzardi* Infections.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 3. pp. 613–626.

"*Filaria bancrofti*. . . . The presence of the adult worm in the varico-lymphocoele of the cord is constant. The site where the worms are found is always the same, viz., in the distal portion of the lymphatic plexa of the cord, in proximity to the epididymis. . . . The author has not been able to find adult living worms in any other situation, nor to observe, in any other district of the lymphatic system, the lesions which are characteristic of invasion by the adult worm.

"*Filaria ozzardi*. On no occasion were any traces of adult worms seen nor was there observed any pathological change in the lymphatic system of those infected with *F. ozzardi*."

The paper summarizes the conclusions drawn from the clinical and pathological findings in over 7,000 cases. It is confirmed that in British Guiana *Wuchereria bancrofti* is limited to the coastal district. It affects, as evidenced by microfilariae in the blood, 40 per cent. of negroes

and Portuguese, 20 per cent. of East Indians, and few Chinese, is rare under 10 years of age, is periodic in direct relation to the intensity of the infection with the higher count at night, the physical signs affecting the lymph glands are mainly confined to those draining the genital organs, especially to the "mesial superior group of the superficial subinguinal lymph glands," varicolymphecele is constant in the male and an "elephantoid condition of the broad and ovarian ligaments" in the female.

Filaria ozzardi is confined to the interior; race, sex and age do not influence it; is without variation of the microfilarial count from day to day and hour to hour, and causes no physical signs. *Mf. bancrofti* was found in no fluid, ascitic, synovial, cystic, other than in cysts connected with the cord or internal female genital organs; *Mf. ozzardi* has been found only in the peripheral blood in admittedly incomplete examinations. The site of adult *W. bancrofti* in Romiti's view is as quoted above. Since from tissue removed at operation and placed in warm saline adults, if present in patent lymphatics, emerged with rapid twisting movements, it is held logical to conclude that the same holds after death and that the worms then migrate from superficial into deep lymphatics. No adults of *F. ozzardi* were seen, nor was any pathological change in the lymphatic system attributable to them discovered. In both infections bacteria were not discovered apart from acute inflammation and then the organism was predominantly *Staphylococcus pyogenes aureus*. C. L.

NEUBER (Eduard). Beiträge zur Diagnose, Epidemiologie und Therapie der Filariase (*Filaria bancrofti*) auf Grund zweier Fälle. [Two Cases of *W. bancrofti* Infection. Treatment.]—*Arch. f. Dermat. u. Syph.* 1935. May 31. Vol. 171. No. 5. pp. 515–525. With 3 figs.

Two cases are described in whom the scrotum and penis showed lymphangiectatic vesicles and who were treated with malaria and gold. In both it is stated that microfilariae were present in the blood. In one the microfilariae disappeared and the lymphangiectasis lessened. The other is under observation. C. L.

DAVIS (Nelson C.). An Investigation of Possible Vectors of *Wuchereria bancrofti* (Cobbold) in Bahia, Brazil.—*Jl. Parasitology*. 1935. Feb. Vol. 21. No. 1. pp. 21–26. [10 refs.]

The chief transmitter of *W. bancrofti* infection in Bahia, Brazil is *Culex fatigans*.

"1. Experimental proboscis infections with *Wuchereria bancrofti* (Cobbold) were obtained in the following mosquitoes: *Culex fatigans* Wiedemann, *Mansonina* (*Rhynchotaenia*) *justamansonina* (Chagas), and *Anopheles* (*Nyssorhynchus*) *albitalis* Arribáizaga.

"2. Advanced development of larvae took place occasionally in *Anopheles* (*Nyssorhynchus*) *bachmanni* Petrochi and in *Culex nigripalpus* Theobald. Retarded development was also noted in one specimen of *Anopheles* (*Nyssorhynchus*) *tarsimaculatus* Goeldi.

"3. A slight degree of development, followed by degeneration, occurred in *Aedes* (*Stegomyia*) *aegypti* (Linnaeus) and in *Aedes* (*Ochlerotatus*) *fluviatilis* (Lutz).

"4. No metamorphosis was noted in *Aedes (Ochlerotatus) taeniorhynchus* (Wiedemann) or in *Aedes (Ochlerotatus) scapularis* (Rondani). Invasion of the thorax occurred only once in *Aedes taeniorhynchus* and never in *Aedes scapularis*." C. L.

NEUBER (Eduard). Ueber den Heilwert und Wirkungsmechanismus der Goldpräparate, mit besonderer Rücksicht auf einige chronische Infektionskrankheiten (Sklerom, Aktinomykose, Filariase). [**Curative Value of Gold Preparations with Special Reference to Filariasis.**]—*Wien. Klin. Woch.* 1935. Apr. 19. Vol. 48. No. 16. pp. 486–490. [13 refs.]

Gold had no influence on 2 cases of infection with *F. bancrofti*. After combination with malaria one was cured 4 years later. C. L.

TISSEUIL (J.). De la longévité des microfilaires de la sarigue *Philander* dans la circulation générale. [**Longevity of Microfilariae of Opossum in Circulation.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 193–194.

A single microfilaria was found 6 and 11 days respectively after blood rich in embryos had been injected into the peritoneal cavities of two other opossums [see TISSEUIL, this *Bulletin*, Vol. 32, p. 278]. C. L.

MONTEL (M.). Le carbone animal intraveineux dans le traitement des rechutes aiguës fébriles de la lymphangite chronique éléphantiasigène des pays chauds. [**Animal Charcoal Intravenously in the Treatment of Acute Relapses of Chronic Lymphangitis.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 171–174.

A severe case of lymphangitis responded dramatically to intravenous injections of animal charcoal.

A man of 45 had had for 10 years lymphangitic attacks which had left permanent enlargement of the right leg. The three attacks which Montel had observed never retrogressed before the 8th or 10th day, and necessitated a slow convalescence. In the last the temperature reached 40.5°C., with shivering, delirium, pulmonary congestion, lymphangitis in the right leg and corresponding painful adenitis. An intravenous injection of 5 cc. of a 2 per cent. suspension of finely ground animal charcoal in physiological (normal) serum on the second day and one of 10 cc. on the third day were followed by a return to 37°C. (98.4°F.) on the fourth day, with a recovery of well-being so complete that the man insisted on taking forthwith a business journey of 400 km. by car. He took 15 cc. ampoules for daily injections and supported the journey well. C. L.

MARTÍNEZ-BÁEZ (M.). Sur la structure histologique des nodules à *Onchocerca volvulus* et *O. caecutiens*. [**Histological Structure of Onchocerca Nodules, Volvulus and Caecutiens.**]—*Ann. Parasit. Humaine et Comparée.* 1935. May 1. Vol. 13. No. 3. pp. 207–230.

A comparative study of the structure of onchocerca nodules, based on 21 specimens from Africa and 28 from America, described in detail, though the author's experience covers 61 specimens in all.

The skin over nodules is never normal. The epidermis is practically so; the dermis never, having very often an oedema, and always showing numerous foci of cellular infiltration, most markedly so in deeper layers. These are apt to form sleeves round dilated blood and lymph vessels, and comprise lymphocytic, histiocytic, plasmocytic and eosinophilic types. The nodules are almost always sharply delimited by a fibrotic capsule composed of concentric collagenous fibres often undergoing hyaline degeneration, the spaces between being occupied by macrophages, histiocytes, lymphocytes, some polynuclears and eosinophils and a few labrocytes and often harbouring microfilariae. The uteri contain the young, which may be in various stages from egg to fully developed larva, but it is particularly noted that, when the latter are present in the uteri, there are abundant microfilariae in the tissues of the nodule and in the superjacent skin [an observation which suggests that in onchocerca the parturition of each female takes place when the products of parturition fill the uteri]. In one case there were in the nodule microfilariae of double the normal length as described by OCHOTERENA. In the same nodule there may be found normal and disintegrating adult worms, and of the cellular elements giant cells were generally very numerous particularly in nodules from America.

The differences discovered between nodules from the old and new worlds are tabulated thus, it being noted that their structure is essentially the same, and that the observed differences need further investigation.

	" <i>O. volvulus</i> ."	" <i>O. caecutiens</i> ."
Perivascular infiltration of the dermis ...	Little accentuated	Marked
Microfilariae in the overlying dermis ...	Many	Few or absent
Granulomatous tissue in the centre of the nodule	In small areas	In larger areas
Local eosinophilia	Frequent and intense	Frequent but light
Dead and living parasites in the same nodule	Frequent	Not seen
Cavities with fibrinous fluid	Frequent	Rare
Cavities with purulent fluid	Rare	Frequent
Disintegrating worms	Frequent	Rare

BRYANT (J.). Endemic Retino-Choroiditis in the Anglo-Egyptian Sudan and its Possible Relationship to *Onchocerca volvulus*.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 523–532. With 1 map & 5 figs. on 2 plates.

Two ocular conditions are associated with devastating blindness in the Sudan, of which one is certainly and the other inferentially caused by onchocerca infection. The infection has been endemic for years, but has recently taken on epidemic character.

About 4 years ago Bryant's attention was drawn to one of these conditions which he calls "Sudan blindness," the lesion being gross retino-choroiditis with optic atrophy. HISSETTE suggesting that it might be due to *O. volvulus*, further investigation has shown blindness

to be appallingly common in places. Thus 8 per cent. of Dinka taxpayers were exempted for blindness contracted during last year; of the Bellanda tribe 4.5 per cent. were totally blind; 8 blind were found in a family of 13 on the Naam river, 14 of 21 in 4 huts near Wau, 4 of 6 in the Tonj district. Most of these were due to retino-choroiditis but some, definitely, to onchocercal punctate keratitis.

To take the latter first, the onset is with intense irritation (even severe pain) and enduring lachrymation. A case seen a month after onset showed dilated pupils, some loss of corneal lustre, oedematous and rather red conjunctiva, fundus covered with pigment patches, optic disc pink and rather indistinct in outline. Vision is usually better in early morning and late afternoon when glare is less, the eyes are shielded, the man keeps in the shadow and tears stream down his cheeks. The media become opaque and adhesions slowly obliterate the pupil. Microfilariae have always been present on puncturing the anterior chamber under 2 per cent. pantocaine with a tuberculin syringe. On sectioning the eye microfilariae are found throughout it, the cornea is vascular, the sclerotic and choroid show a plasma cell reaction, the ciliary body marked inflammatory and fibrotic change.

As for Sudan blindness the slight initial irritation and lachrymation end usually within 3 weeks, when night blindness becomes established. The eye looks normal, but within 2 to 5 months blindness is established. The media are clear, though cataract is not uncommon. Microfilariae are not found on puncturing the anterior chamber. The appearance of the fundus with its patches of retinal pigment, this tissue being otherwise rarified allowing the choroidal vessels to shine through it, is illustrated. On sectioning, microfilariae were entirely absent, the cornea, ciliary body and choroid showed no inflammation, the retinal layers, especially that of nerve fibres, are irregularly atrophied and the cell layers lessened in numbers, the retina shows pigment masses on, and within, it, and its vessels are more numerous than usual, but have no cellular reaction round them.

As to the first condition, the presence of intraocular microfilariae and of onchocerca nodules leaves no doubt as to its causation. As to the second Bryant gives reasons for excluding as causes organic poisons, antimony as a cosmetic, nephritis, diabetes, yaws, eating of cassava root to excess, heredity, consanguinity, famine and vitamin A deficiency; but a possible association with *Onchocerca volvulus* is suggested by the following. Of 750 adults paraded for sleeping sickness inspection 9 per cent. showed manifestations of this infection namely thickened skin, onchocercal tumours, keratitis, hydrocele, and elephantiasis. The last two are included because *W. bancrofti* is unknown here and because *Mf. volvulus* has been found in swarms in elephantoid tissue and in hydrocele fluid and sac. On the other hand, of a number of cases of "Sudan blindness" 58 per cent. showed these visible evidences of *O. volvulus*, or 49 per cent. more than the average of the adult population.

As to tumour distribution the author agrees with HISSETTE that tumours on the head are more apt than others to give rise to the known ocular manifestations of *O. volvulus*, and records that the nodules may produce deep erosion of the frontal bone.

Simulium damnosum is common, indeed at times is a swarming scourge, was present in hundreds in a rest house kitchen 1 km. from water, and appeared to be thoroughly domestic, none being found outside on the road.

C. L.

BOASE (A. J.). **Ocular Filariasis.**—*East African Med. Jl.* 1935. Jan. Vol. 11. No. 10. pp. 326-328.

Case of a Muganda whose left eye was sightless with evidence of kerato-iritis, the right having vision 6/5 and microfilariae in the anterior chamber.

The history was acute. It appears that both eyes began to water and ache, the right became apparently normal in a few days, the left deteriorated rapidly and its sight was lost in 6 weeks. Examination 4 months after the onset "revealed nothing abnormal in the right eye except evidence of past papillitis. . . . The left eye showed intense ciliary congestion, a very hazy cornea, profuse keratitic precipitate (visible to the unaided eye), and posterior synechiae. The fundus was completely obscured." Examination of the right eye with a corneal microscope revealed many nematode larvae. The description is as follows :—

"Prolonged examination revealed many of these organisms. At one instant four were in focus in close proximity to each other, while rapid movements of the beam of light across the anterior chamber disclosed others. The manner in which they propelled themselves through the aqueous immediately suggested to my mind the well-known antics of the mosquito larva, though I think that a better description of their movements would be to say that they tied themselves into knots and untied themselves with amazing rapidity. For this reason it was difficult to form an estimate of their individual length, but in a few instances in which a larva (for such they were deemed to be) was momentarily straightened out a rapid comparison led me to judge its length to be approximately equal to the depth of the optical section of the cornea, that is about a third of a millimetre."

Mf. perstans was present in the blood, but the embryos were not found in the eyes of other patients in whose blood they were present. [The history, the ocular symptoms (*cf.* BRYANT, above) and the estimated size of the microfilariae are suggestive of infection with *Onchocerca volvulus*. The grave blinding effects of this worm, not only in the Belgian Congo but in the Sudan, must give rise to anxiety as to whether the case cited is not the first reported evidence of its presence in Kenya Colony. The existence of nodules is not mentioned.] C. L.

PRESTON (P. G.). **Report of a Case of Human Onchocerciasis in Kenya.**—*Jl. Trop. Med. & Hyg.* 1935. Apr. 1. Vol. 38. No. 7. p. 81.

This is believed to be the first case of onchocerciasis microscopically identified in Kenya.

The man had always lived in South Mugrango in the Kisii Reserve except for service as a porter with the King's African Rifles near Kili-manjaro during the Great War. He had four swellings on the left side of the chest, in both axillae, both iliac fossae, both popliteal fossae, and under the left angle of the lower jaw. On excision the swellings contained onchocerca worms. The man had complained of pain in the temporal region as if a knife were thrust into the backs of his eyes, and stated that he had had occasional and temporary blurring of vision and that this was now becoming impaired. The swellings were of about 2 years duration and had steadily grown. Vision and eye grounds are not reported on. C. L.

ISSAJEV (L. M.). Einfache Methode zum Nachweis der Nematoden-Larven in den Crustacea. [**A Simple Method for the Detection of Nematode Larvae in Crustaceans.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian. pp. 238–240. German summary p. 240.]

Working on the transmission of guinea-worm larvae by cyclops, the author devised the following method for the rapid examination of large masses of these crustaceans. Captured cyclops are placed in test-tubes from which most of the water is pipetted off and which are kept at 35–36°C. for 1–2 days, after which the contents are examined under a microscope at a magnification from 25 to 75. By this time the majority of the crustaceans are macerated and broken up, while the *Dracunculus* larvae retain their normal structure and can easily be detected. This method is based on the fact that under natural conditions the larvae escape into the outer world only after the death and decomposition of their vector. It is suggested that it might be applied for the examination of crustacean vectors in the case of the larvae of other nematodes and cestodes.

C. A. Hoare.

ISSAJEV (L.). Ueber die Eindringung der *Dracunculus medinensis*-Larven in den Cyclops. [**On the Method of Penetration of the Guinea-Worm Larvae into Cyclops.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian. pp. 212–230. With 13 figs. [20 refs.] German summary p. 230.]

Working in Turkestan the author conducted a series of experiments with the view to determine the method by which the larvae of *Dracunculus medinensis* penetrate into the local vectors, *Cyclops oithonoides* and *C. vicinus*.

The copepods and the nematode larvae were placed together in watch-glasses containing distilled or filtered pond-water and were observed under a microscope. The cyclops actively hunts the larvae and ingests them. To facilitate the observation of the larvae within the body of the crustaceans, these were starved and placed between slide and coverslip sealed with vaseline. About 5–6 hours after ingestion, but sometimes after a few minutes, the larvae pass into the body-cavity of the cyclops by actively boring head first through the stomach wall. Active penetration of the larvae through the integuments of cyclops could not be observed under the most favourable conditions. Similar experiments conducted with a number of Cladocera showed that they were incapable of ingesting guinea-worm larvae, while those taken up by *Diaptomus* passed through its intestine and were discharged from the anal aperture unaltered. The paper contains a detailed illustrated account of the structure of the alimentary tract of cyclops and of its feeding methods.

C. A. Hoare.

ISSAJEV (L.). Experimentelle Dracunculosis beim Hunde. [**Experimental Dracontiasis in Dogs.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian. pp. 231–238. With 5 figs. German summary pp. 237–238.]

Description of the results of experimental infection of dogs with *Dracunculus medinensis* undertaken in Turkestan between 1927 and 1932. Pups from 4 to 6 months old were starved for 24 hours and each given 100 cc. of water in which were infected cyclops, containing a total

of 25-50 guinea-worm larvae, the last having moulted twice. Of 42 pups 27 became infected. Dissection of the worms at various periods of time (up to one year) following the infective meal showed that its development up to the production of ripe, motile larvae, takes 9-10 months. Males could not be found. In one case cyclops were infected with larvae isolated from a worm obtained in one of the experimental infections; after developing for 13 days in the crustaceans 25 larvae were fed to another pup and gave rise to an infection with 5 adult worms the uteri of which contained motile larvae when examined about 9 months later. It is suggested that the successful experiments coupled with the finding of naturally infected dogs points to the latter as sharing with man the rôle of final hosts. The incidence of dracontiasis in the town of Old Bokhara was 30 of 30,000 of the human population and 5 of 2,023 dogs examined. C. A. Hoare.

RAMSAY (G. W. St. C.). **Observations on an Intradermal Test for Dracontiasis.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Jan. 25. Vol. 28. No. 4. pp. 399-404.

The antigen for the test was obtained from guinea-worm and the results, which were satisfactory, indicated a high rate of infection in Northern Nigeria.

To 100 cc. of ether was added 0.25 gm. of dried powdered guinea-worm with frequent shaking at room temperature for 2 hours to remove lipoids. The dried ether-free residue was extracted, with shaking, for 4 hours in 100 cc. of 0.85 per cent. sodium chloride at 37°C. After centrifuging and passing through a No. 6 Seitz filter, 0.25 cc. of this 0.25 per cent. saline extract was used for injection, a positive wheal being one at least 2.3 cm. across, with outrunners. Of 41 visibly infected cases 85 per cent. gave an immediate positive result. Of 187 persons in a non-endemic area a negative reaction was obtained in 84 per cent. "and a spurious positive reaction in 16 per cent." There was failure to produce an antigen suitable for a precipitin test. Of 1,267 other persons in Northern Nigeria 47.6 per cent. gave an immediate positive reaction, suggesting that this persists for years after infection has ceased, and that in some local areas dracontiasis is hyperendemic. C. L.

MOORTHY (V. N.). **The Influence of Fresh Bile on Guinea-Worm Larvae encysted in Cyclops.** (A Preliminary Report.)—*Indian Med. Gaz.* 1935. Jan. Vol. 70. No. 1. pp. 21-23. With 2 figs.

Bile kills cyclops and activates guinea-worm larvae which they harbour.

Like 0.2 per cent. hydrochloric acid, fresh bile of certain species of the fish genus *Barbus* killed cyclops in 1 to 2 minutes and so activated guinea-worm larvae within that they disorganized the host's internal structure and might escape from its body after 30 to 35 minutes, usually at the junction of the anal segment with the furcal rami. With fresh goat's and sheep's bile the corresponding figures were 30 to 36, and 60 minutes, and in human bile from a suicide 6 hours after death 20 and 79 minutes. In *Barbus* some development of the guinea-worm larva is believed to occur. The work continues. C. L.

Erratum.

Vol. 32, No. 4, p. 246, BEQUAERT's summary, line 3 of title, for *Blandfordia* read *Blanfordia*, and for H. A. PILSBURY read H. A. PILSBRY. Also in text of summary read *Blanfordia* for *Blandfordia* throughout.

- ASHKAR (M. F.) & ISSA (I. I.). Bilharzial Haemospermia.—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 274-283.
- CAWSTON (F. G.). Elephantiasis in South Africa and Basutoland.—*Jl. Trop. Med. & Hyg.* 1935. Feb. 1. Vol. 38. No. 3. p. 34. With 1 fig.
- CHEN (H. T.). A Preliminary Report on a Survey of Animal Parasites of Canton, China, Rats.—Reprinted from *Lingnan Sci. Jl.* Canton. 1933. Feb. Vol. 12. No. 1. pp. 65-74. [10 refs.]
- CHE. (H. T.). On a Method of expelling Disintegrated Tapeworms in *Ctenocephalides felis*.—Reprinted from *Lingnan Sci. Jl.* Canton. 1933. May. Vol. 12. Supp. pp. 43-48.
- CHEN (H. T.) & WANG (Shou-chi). Notes on Some Abnormal *Clonorchis sinensis*.—Reprinted from *Lingnan Sci. Jl.* Canton. 1933. Oct. Vol. 12. No. 4. pp. 541-546. With 4 figs. on 2 plates.
- CHEN (W. L.) & ROSE (G.). Untersuchungen ueber die Verbreitung der Menschlichen Paragonimiasis im Talbezirk von Landin (Provinz Chekiang, Hsien Shaoshing).—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 519-524.
- GRUBER (Georg B.). Zur Frage der Wurmkrankheiten. (Zu Szidat's und Wigand's "Leitfaden der einheimischen Wurmkrankheiten des Menschen.")—*Muench. Med. Woch.* 1935. May 9. Vol. 82. No. 19. pp. 733-735. [13 refs.]
- KHAILIL Bey [Opened by]. A Discussion on the Criteria of Cure from Bilharzia.—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 228-231.
- KHAW (O. K.). Treatment of *Schistosomiasis japonica* in Rabbits with Concentrated Fouadin. (A Preliminary Report).—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 535-541.
- KODZUMI (Makoto). Studies on the Toxic Actions of the Coelomic Fluid of Ascaris.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 589-599. With 4 figs. on 3 plates. [43 refs.]
- KOMIYA (Y.), KAWANA, K. & TAO (S.). Investigations into Helminthiasis among Japanese Pupils in Shanghai.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 611-617.
- KU (D. Y.). Oxyuris Infection of the Wall of the Fallopian Tube.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 605-610. With 2 figs. on 1 plate. [11 refs.]
- MALLIK (K. L. Basu). A Case of Guinea-Worm Infection.—*Indian Med. Gaz.* 1935. May. Vol. 70. No. 5. p. 264. With 1 fig.
- MARTILLOTTI (F.). L'ascaridiosi nell'infanzia.—*Pediatria.* 1935. Mar. 1. Vol. 43. No. 3. pp. 321-331.
- MUELLER (Justus F.). A *Diphylllobothrium* from Cats and Dogs in the Syracuse Region.—*Jl. Parasitology.* 1935. Apr. Vol. 21. No. 2. pp. 114-121. With 21 figs. [10 refs.]
- OHIRA (Tokuzo). On the Active Immunization of Animals against Tape Worms.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 601-604.
- OTTO (J. H.). Clinical Pathophysiological and Therapeutical Aspects of Human Clonorchiasis.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 543-561. [73 refs.]
- OXENIUS (Kurt). Zur Behandlung des Pruritus ani bei Oxyuriasis.—*Muench. Med. Woch.* 1934. Dec. 20. Vol. 81. No. 51. pp. 1977-1978.

- ROSE (G.) & KOH (T. M.). Beobachtungen ueber die Fortpflanzung und die Lebensweise der Zwischenwirtschnecke (*Oncomelania hupensis*) von *Schistosoma japonicum* unter Laboratoriumsbedingungen.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 525–533.
- SCADUTO (Pasquale). Alcuni animali da cortile ed i passeri quali vettori della diffusione a distanza delle uova di *Ankylostoma duodenalis*.—*Riv. Sanitaria Siciliana.* 1935. Apr. 15. Vol. 23. No. 8. pp. 597–600, 603–604. [14 refs.] English summary (5 lines).
- VOGEL (Hans). Der Entwicklungscyclus von *Opisthorchis felineus*.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 619–624.
- YOUNG (Shutsu). The Blood Picture in Human Fasciolopsiasis (*F. buski*).—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 563–566.
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MISCELLANEOUS.

POGGI (Igino). Parassiti intestinali nei bambini: rilievi statistici e note cliniche. [Intestinal Parasites in Children (in Milan).]—*Arch. Ital. Sci. Med. Colon.* 1935. May 1. Vol. 16. No. 5. pp. 321-349. With 1 fig. [34 refs.] English summary (2 lines).

The author examined the faeces of 1,100 children between the ages of 2 and 14 years in the South Corona Hospital, Milan, and found 614 or 56 per cent. harbouring parasites of some kind. [The method of examination is not stated; presumably it was by direct smear.]

These include all forms, even those not regarded as pathogenic such as *Trichomonas intestinalis*, *Entamoeba coli*, *Spirochaetes*, *Blastocystis* and *Bodo*. The commonest was ova of *Trichuris trichiura* found in 298 or 27 per cent., *Ascaris* 158 or 14 per cent., *E. coli* 123, *Blastocystis hominis* 108, and *Giardia* 98. *E. histolytica* was found in 7 or 0.6 per cent., *H. nana* in 10 or 0.9 per cent. Helminthic infestations were commonest at the age of 7 years, being found in 39 of 76 children at that age; almost the same proportion, 44 out of 91 and 39 out of 78, was found at ages 6 and 10 years. Details are given of 15 patients. There is no mention of any having resided outside Milan. H. H. S.

PECKOLT (Waldemar) & PRADO (Alcides). Contribution au traitement des protozooses intestinales par le *Jacaranda decurrens* Cham. (*Bignoniaceae*). [Treatment of Intestinal Protozoal Infections by *J. decurrens*.]—*C. R. Soc. Biol.* 1934. Vol. 117. No. 33. pp. 719-720.

Tincture of Carobinha prepared from the South American plant *Jacaranda decurrens* Cham. has, in the authors' hands, given good results in the treatment of giardia, chilomastix and trichomonas infections and even results which may be regarded as encouraging with amoebic dysentery. The tincture has a pleasant taste and is quite non-toxic.

C. M. Wenyon.

BALENA (Alfredo). Giardiose biliar. [Biliary Giardiasis].—*Brasil-Medico.* 1935. Jan. 19. Vol. 49. No. 3. pp. 47-56. With 1 chart. [11 refs.] French summary.

The study of 19 cases of giardia infection by radioscopy of the gall bladder and examination of the bile obtained by duodenal tubage has convinced the author that a condition of cholecystitis caused by the flagellates in the gall bladder exists. The symptoms are varied and may resemble those due to ulceration of the stomach, the presence of biliary or renal calculi, or cardiac disturbances as revealed by arrhythmia or angina. Various lines of treatment are recommended but it is admitted that it is not easy to eradicate the parasite. The conclusion that the parasites actually inhabit the biliary passages is somewhat equivocal, for the author admits that they were not found in the gall bladder in cases which were treated surgically. [The discovery in bile obtained by duodenal tubage of a flagellate, known to live and reproduce in large numbers in the duodenum, would hardly seem to justify the assumption that it has necessarily come from the gall bladder. There appears to be a growing tendency in the literature to attribute to this flagellate serious pathogenic properties based largely on this

assumption. The records of the discovery of giardia in the gall bladder itself at the time of surgical interference are as yet far from convincing.]

C. M. W.

FILLION (H.) & MILLISCHER (P.). La résine du *Schinus terebenthifolius* dans le traitement de la lamblia. [*Resin of S. terebenthifolius in Treatment of Giardiasis.*]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 92-97.

The author claims that the product of distillation of the resin of *Schinus terebenthifolius*, a colourless essence, has a specific action on lamblia infections, when administered by the mouth in doses of 1 to 4 cc. daily in a mixture containing paregoric, syrup of tragacanth and julep. In discussion DESCHIENS points out that temporary disappearance of flagellates and their cysts from the stool is a common occurrence without treatment, so that care is required in drawing conclusions as to the action of any drug administered.

C. M. W.

GRAMS (H.). Beitrag zur Lamblienerkrankung. [*Giardiasis.*]—*Klin. Woch.* 1934. Dec. 15. Vol. 13. No. 50. pp. 1796-1797. [13 refs.]

SINCKE (G. E.). Zur Therapie der Lambliosis. Bemerkungen zur Mitteilung von H. Grams, Beitrag zur Lamblienerkrankung, in Jg. 1934, S. 1796 dieser Wochenschrift.—*Ibid.* 1935. Feb. 9. Vol. 14. No. 6. p. 204.

In the first paper 3 cases of lamblia infection are described, two of which were cured, one by a single neosalvarsan injection of 0.6 gm. and the other by duodenal lavage with magnesium sulphate and olive oil combined with neosalvarsan injection of 0.3 to 0.6 gm. The third case proved refractory to all the treatments tried.

In the second paper the author records failure to cure lamblia infections by neosalvarsan injection but success by introduction of the salvarsan solution (0.3 to 0.45 gm. in 200 cc. water) into the duodenum.

C. M. W.

DOBELL (Clifford). *Researches on the Intestinal Protozoa of Monkeys and Man. VI. Experiments with the Trichomonads of Man and the Macaques.*—*Parasitology.* 1934. Oct. Vol. 26. No. 4. pp. 531-577. [44 refs.]

After a number of carefully controlled experiments with the trichomonads of man and macaques the author arrives at the general conclusion that the intestinal and vaginal trichomonads of man are not specifically distinct from one another nor from the flagellates of similar habitat in macaques. The consequence of this is that *Trichomonas vaginalis* Donné, 1837, *T. hominis* Davaine, 1860 [= *T. intestinalis* Leuckart, 1879] and *T. macacovaginae* Hegner and Ratcliffe, 1927 are synonymous. Within this species there exist diverse strains distinguishable by minor morphological characters (size, average number of anterior flagella, etc.) and physiological properties (infectivity for various hosts, ability to ingest red blood corpuscles, etc.). In these experiments a human being, the author himself, was infected with an intestinal trichomonad from a monkey, the infection produced being a typical *T. hominis* infection which has persisted for 4½ years. With

this same strain a monkey free from intestinal trichomonad infection was given a vaginal infection which has been in existence for 3½ years. [Though in no case was the author able to infect a monkey with a trichomonad of human origin, the experimental infection of man with a monkey strain, noted above, and the cross infection experiments between monkeys of different species can leave no doubt that the general conclusions drawn by the author are correct.] C. M. W.

HEGNER (Robert) & ESKRIDGE (Lydia). **Elimination and Cross-Infection Experiments with Trichomonads from Fowls, Rats and Man.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 135–150.

A 1 per cent. carbarsone in 1 per cent. sodium bicarbonate solution given to rats in place of water will eliminate all trichomonads from the intestine in 5 days. Each rat ingested about 0.1 gm. carbarsone a day. Other protozoa (amoeba, giardia, hexamita and chilomastix) were not affected to any considerable extent. The solution administered to chicks eliminated a caecal trichomonad infection in 1 to 7 days. They could be reinfected immediately after the treatment was discontinued. Trichomonas-free rats were infected with *Trichomonas hominis* in culture, the infection lasting at least for 61 days in some cases. Clean rats became infected with rat or human trichomonads when made to associate with infected rats. C. M. W.

WESTPHAL (Albert). Das Verhalten von *Trichomonas vaginalis* in der Kultur. [**Behaviour of *T. vaginalis* in Culture.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 106–112. With 5 text figs. [13 refs.]

By a special technique the author has succeeded in maintaining *Trichomonas vaginalis* in culture for 9 months. Compared with the intestinal *T. hominis* it exhibits structural differences which justify its retention as a distinct species. C. M. W.

HEGNER (Robert) & ESKRIDGE (Lydia). **Influence of Carbohydrates on Intestinal Protozoa in Vitro and in Vivo.**—*Amer. Jl. Hyg.* 1935. Jan. Vol. 21. No. 1. pp. 121–134. With 1 chart. [18 refs.]

The estimation, chiefly by a colour reaction, of the quantity of starch in 94 specimens of human faeces did not show that there existed any relation between the quantity of starch and the protozoal infections present. In cultures of *Trichomonas hominis* the flagellate growth is greatly improved by the addition of rice starch. C. M. W.

BRUMPT (E.). Au sujet de la prétendue schizogonie régressive des gamètes femelles d'*Haemoproteus paddae*: présentation de préparations. [**The Alleged Regressive Schizogony of Female Gametes of *H. paddae*.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 144–154. With 8 figs. [30 refs.]

In this illustrated article the author discusses the references which have been made in the literature to the subject of the possible schizogony of the female gametocytes of halteridium of birds. He shows conclusively that a failure to recognize the existence of double infections of plasmodium and haemoproteus, and the apparent fusion in the red

blood corpuscle of a number of parasites when multiple infections occur, are responsible for the opinion that schizogony of gametocytes may take place.
C. M. W.

MAGATH (Thomas Byrd). **The Coccidia of Man.**—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 91-129. With 3 figs. [129 refs.]

In this lengthy discussion of the subject of coccidiosis in man it is pointed out that there is no proof that any species of *Eimeria* inhabits the body of man as a parasite. Of the *Isospora* there is one species, which the author argues (in the reviewer's opinion fallaciously) should be known by the name *Isospora hominis* Fantham, 1917. Owing to the low incidence of infection with this parasite, which is not adequately separated, in the author's opinion, from the similar parasites of cats and dogs, the suggestion is made that some reservoir host may exist. A list is given of all the previous records of *I. hominis* infection, with a new one from the territory of Hawaii. The question of the nomenclature of this parasite is admittedly involved and it is not clear that the author's arguments solve the difficulties associated with it.

C. M. W.

METELKIN (A.). **The Role of Flies in the Spread of Coccidiosis in Animals and Men.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. Nos. 1-2. [In Russian. pp. 75-82. English summary p. 82.]

The author carried out a number of experiments with a view to establishing the possible epidemiological rôle played by flies in the dissemination of coccidial infection. Various laboratory-bred and "wild" flies (*Musca domestica*, *Calliphora erythrocephala*, *Lucilia caesar*, *Cynomyia mortuorum*, *Stomoxys calcitrans* and *Phormia groenlandica*) were fed on the faecal suspensions of rabbits containing coccidial oöcysts. These were subsequently examined in the droppings and oral discharges. It was found that all the flies were capable of ingesting the oöcysts, which remained unaltered and viable in the intestinal contents up to 24 hours, and in the discharges until the latter dried up. Oöcysts were also recovered from the external parts of the body of the insects. The viability of the oöcysts was tested by the eosin-staining reaction and by their capacity to sporulate in a solution of potassium bichromate. The length of time during which the oöcysts remain viable in the gut of the flies, the rate at which these discharge the intestinal contents and the range of their flight (700 metres in the case of the house-fly), are all epidemiological factors suggesting that these insects play an important rôle in the mechanical transmission of coccidiosis.
C. A. Hoare.

TAYLOR (Frank H.). **A Check List of the Culicidae of the Australian Region.**—*Commonwealth of Australia Dept. of Health, Service Publication (School of Public Health & Trop. Med.) No. 1.* 1934. May 25. 24 pp. With 1 folding map.

The list enumerates the mosquitoes, including *Dixa*, *Chaoborus*, etc., known to occur in Australia and New Zealand and in the islands from the Celebes and Moluccas on the west to the Marquesas on the east.

The pamphlet is interleaved with plain paper and includes a map of the region.

The list is based on EDWARDS' Culicidae in "Genera Insectorum," but the information on geographical distribution is much more complete and thoroughly up-to-date. There is one error which is of considerable medical importance and to which attention must be called. The author (apparently copying EDWARDS) includes New Caledonia in the range of *Anopheles punctulatus*. We can find no evidence for the insect occurring there either in collections in this country or in the papers to which the author refers in his bibliography.* We think that the mosquitoes of New Caledonia are fairly well known and believe that the island is free of *Anopheles* and of indigenous malaria.

P. A. Buxton.

LI (Feng-swen) & Wu (Shih-cheng). **The Mosquitoes of Hangchow, Chekiang.**—Year Book No. 3, Bur. Entom., Hangchow (1933). 1934. pp. 97–123. With 3 plates.

According to the authors of this compilation, twenty-seven species of mosquitoes, including four anophelines (*Anopheles aitkeni*, *A. hyrcanus* var *sinensis*, *A. lindesayi* and *A. minimus*) have been met with at Hangchow. Included in this total, however, is *Aedes scutellaris*, as to which the present reviewer is informed by Dr. F. W. EDWARDS that Messrs. Li and Wu are in error, since that species "is not known to occur in China, and almost certainly is not to be found there."

In the present publication, which should be locally useful, brief diagnostic characters and notes on distribution are given for each species mentioned, with in addition, where such records exist, data as regards "Sanitary importance."

E. E. Austen.

HANCOCK (G. L. R.). **The Mosquitoes of Namanve Swamp, Uganda. With an Appendix on the Estimation of Organic Carbon in Waters** by G. GRIFFITH.—*Jl. Animal Ecology*. 1934. Nov. Vol. 3. No. 2. pp. 204–221. With 4 figs. on 3 plates. [11 refs.]

The paper sets out observations, both biological and physico-chemical, on the mosquito larvae which occur in and about a large swamp containing papyrus.

The problem which the author has undertaken is an extremely complex one, for in a period of one year he discovered 35 species of mosquito in his swamp and he refers them to eight types of habitat. He is able also to contrast the fauna of his swamp with that of forest pools. The physico-chemical factors were not studied at regular intervals, but a considerable number of observations are recorded. In spite of the fact that the swamp is permanent, it is interesting to observe that the numbers of certain species show marked seasonal prevalence. For instance, there was an increase of larvae of *Anopheles gambiae* after rain. In the author's view, the numbers of these were reduced during the dry season owing to the higher organic content of the water. When the rain fell and diluted the water, it became more suitable to larvae of this insect. It seems that more rapid progress in our understanding of the ecology of mosquitoes might be made if workers would test their ideas experimentally.

* In a letter recently received Mr. Taylor agrees that this is so.

The paper concludes with a note by G. Griffith, describing a method for estimating organic carbon in water. The method can be applied to the water sample itself, and not to the residue left after evaporation.

P. A. Buxton.

DOVE (W. E.) & HALL (D. G.). **Dikes and Automatic Tide Gates in Control of Sand Flies and Salt Marsh Mosquitoes.** [Abstract.]—*Jl. Parasitology*. 1934. Dec. Vol. 20. No. 6. pp. 337-338.

"Sandfly and salt marsh mosquito breeding places are being eliminated at Savannah, Georgia, by the use of dikes fitted with automatic tide gates. The gates close to prevent tidal waters from entering the diked areas but open to permit surface drainage of these areas. In Chatham county where 36 principal breeding places were eliminated by dikes and automatic gates, there has been a marked reduction in the population of both sandflies and salt marsh mosquitoes. Isolations of sandfly larvae from soil samples and the sandflies emerging in field cages show that actual drying of the breeding places either destroys sandfly larvae or concentrates them in the wet soil of the ditches. Observations on the populations of both sandflies and salt-marsh mosquitoes suggest a reduction of 60 per cent. to 75 per cent. of the numbers usually encountered in this county. In view of the fact that only about 30 per cent. of the work is completed in Chatham county, the results suggest a high degree of control."

REV. HORT. AGRIC. AFR. N. Algiers. 1934. Sept. Vol. 38. No. 9. p. 260.—La destruction des moustiques par les cactus épineux. [Mosquito Control by Prickly Pear.]—[Summarized in *Rev. Applied Entom.* Ser. B. 1934. Dec. Vol. 22. Pt. 12. p. 233.]

"Good results in mosquito control have been obtained by means of a mucilaginous mixture made by steeping in water the chopped leaves of prickly-pear (*Opuntia vulgaris*). The mixture floats on the surface of pools and gradually obstructs the tracheae of the larvae, killing them in from 15 to 50 hours. Further, the adult mosquitos seldom oviposit on the water, and if they do, the eggs cannot develop. If the leaves are not steeped but are merely cut up and thrown into the water, the result is the same though slower. This treatment has been found as effective as oiling, and has the advantage of not affecting fish."

OKOUNEVSKI (J.) & KHAKHAIEVA (V.). La volatilité et évaporabilité des désin[s]ectants. [The Volatility and Rate of Evaporation of Insecticides.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 1. pp. 82-91. [In Russian. French summary p. 91.]

The authors have studied some of the physical properties of a number of insecticides from the point of view of their practical application.

Their efficiency depends upon the lethal concentration of the chemical and upon the rate at which it is capable of producing the required concentration. This is determined by the volatility and rate of evaporation of the substance in question. These properties were examined in various insecticides and it was found that the most suitable substances for use at room temperature are carbon tetrachloride and benzene, since they possess a high degree of volatility and a low boiling point (below 120°C.). On the other hand, substances with a higher boiling point (120-180°C.) and a medium rate of evaporation, such as the xylols and solvent naphtha, can only be utilized at very high temperatures.

C. A. Hoare.

CAMPBELL (F. L.), SUELLIVAN (W. N.), SMITH (L. E.) & HALLER (H. L.).
Insecticidal Tests of Synthetic Organic Compounds—Chiefly Tests of Sulfur Compounds against Culicine Mosquito Larvae.—*Jl. Econom. Entom.* 1934. Dec. Vol. 27. No. 6. pp. 1176–1185.

The object of this work was to test a number of synthetic compounds—chiefly sulphur compounds—for insecticidal powers. Culicine larvae were considered a convenient material for the preliminary testing, but use against other insects including terrestrial forms is also contemplated. The substances were applied in the form of extremely dilute solutions, often more nearly suspensions since the substances were of very low solubility. Sixty-eight compounds, mostly solids, were tried in all.

Larvicidal activity was tested against *Culex pipiens*, L., *C. territans* Walk., and *C. quinquefasciatus* Say., in Erlenmeyer flasks containing 100 cc. distilled water and 50 or 100 3rd or 4th instar larvae at a standard temperature (29.3 ± 0.1). The compounds were rejected if less effective than nicotine, that is if killing less than 65 per cent. in 8 hours at a dilution of 1 : 10,000. Twenty-four of the compounds—benzo-thiazoles, disulphides, sulphides, thioethers and thiophenols—were further studied, but 11 further were rejected as not killing 50 per cent. overnight at 1 : 40,000. The most active substances were tested again at dilutions of 1 : 100,000 and 1 : 200,000. The order of activity is not necessarily the same at all dilutions.

Replacement of sulphur in the molecule by oxygen in general resulted in formation of a substance inactive at 1 : 40,000; diphenylene oxide was a noteworthy exception, being slightly more toxic than diphenylene sulphide. These substances were the most toxic, killing nearly 100 per cent. of the larvae in 5 hours at 1 : 200,000. (In an addendum it is noted that thiodiphenylamine (phenothiazine) is even more toxic, functioning at 1 : 1,000,000.)

Larvicidal activity against *Culex* was found to be no criterion of activity against other insects. Several examples of anomalies are given.
D. R. P. Murray.

NIESCHULZ (Otto) & DU TOIT (René M.). **Handling Mosquitoes for Experimental Purposes under South African Conditions.**—*Onderstepoort Jl. Vet. Sci. & Animal Industry.* 1934. July. Vol. 3. No. 1. pp. 79–95. With 5 figs.

Though primarily interesting to veterinarians, this paper contains information of value to all who require to keep mosquitoes alive, especially in dry climates where day temperatures reach a high level.

Throughout work on mosquitoes as vectors of horsesickness and blue-tongue in sheep, the chief difficulty was the maintenance of humidity high enough to suit the insects. With this end in view, the mosquitoes were kept either in small jars covered with mosquito netting, or in cages similarly enclosed. The former "were placed on wet cotton wool in slightly larger jars provided with loosely fitting lids." The wooden tops of the cages were protected by galvanized iron, and tops and sides were draped in a hessian cover, wetted by a constant flow of water. Before being required for use, the mosquitoes (*Aedes* spp.) were fed by large balls of cotton wool saturated in a 10 per cent. solution of sugar water, encased in mosquito netting, hung from the roofs of the cages,

and changed and sterilized on alternate days to prevent moulds. Ingenious arrangements for feeding the mosquitoes on animals are described.

E. E. Austen.

BUCKNER (James F.). **An Improved Technique for mounting Mosquito Larvae.**—*Amer. Jl. Trop. Med.* 1934. Sept. Vol. 14. No. 5. pp. 489–491.

Instead of the customary, but distorting and damaging method of immersion in hot water, it is recommended that mosquito larvae for mounting be subjected to a somewhat lingering (four hours for siphonate, two hours for asiphonate larvae) death in 2 per cent. cocaine hydrochloride solution. The methods of preliminary cleansing in 1·5 per cent. magnesium sulphate solution, and subsequent preparation for mounting are described. For the composition of cells in which to mount specimens in any desired medium the following formula is given.

	Grams.
Beeswax	25
Paraffin (melting point 60° to 62°C.)	10
Gum mastic	6
Prepared chalk	2
Vermilion (for colour)	4

The gum mastic is to be powdered, mixed with the last two ingredients, and the mixture added to the first two after the latter have been melted. The whole should then be allowed to simmer and be stirred for fifteen minutes.

It is claimed that cells so composed will withstand extremes of heat and cold.

E. E. A.

WEYER (Fritz.) *Der Einfluss der Larvalernährung auf die Fortpflanzungsphysiologie verschiedener Stechmücken.* [**The Influence of the Nutrition of the Larvae on the Reproductive Physiology of Certain Mosquitoes.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Sept. Vol. 38. No. 9. pp. 394–398.

The paper describes experiments the purpose of which is to discover whether the food which is given to mosquito larvae has much effect on the biology of the adults, and in particular on their reproductive powers.

The author describes experiments in which larvae of *Culex pipiens* were fed on different diets including powdered liver. On this the larvae grew rapidly and produced vigorous adults, which laid a large number of eggs autogenously. But the larvae of the second generation tended to die and produced very weak adults, in many of which the ovaries failed to develop completely. [It is not clear whether this result was obtained consistently or once.] In similar experiments with *C. fatigans* and *Aedes aegypti*, it was found that the powdered liver gave rise to large vigorous adults, and in a few instances in *A. aegypti* the eggs began to mature without the female receiving a blood meal. The author then applied the same method to *Anopheles maculipennis* of the races *atroparvus* and *messeae*. In *messeae* he observed a commencement of ovarian development in females which had not fed on blood: [this is interesting if it implies that these insects are tending to become autogenous; but if the females had developed from larvae fed on hay

infusion, is it certain that no development of the ovaries would have been observed?] It was also found that male *messeae* suffered from a zoospermia if they had been bred from larvae fed on liver: the development of the sperm in wild males is quite different, and it seems possible that this explains the fact that this race fails to breed in captivity.

P. A. Buxton.

SILVERTHORNE (Nelles) & BROWN (Alan). **Cutaneous Myiasis in Infants.**—*Arch. Dis. in Childhood*. 1934. Dec. Vol. 9. No. 54. pp. 339-342. With 3 figs.

Three cases of cutaneous myiasis produced by the larvae of *Wohlfahrtia vigil* (Walk.) are reported. The lesions occurred in healthy infants sleeping out of doors in June in Montreal. Several references are given to similar cases reported from Canada [see this *Bulletin*, Vol. 30, p. 310].

A. G. B.

AUBERTIN (D.) & BUXTON (P. A.). **Cochliomyia and Myiasis in Tropical America.**—*Ann. Trop. Med. & Parasit.* 1934. Oct. 19. Vol. 28. No. 3. pp. 245-254. With 1 plate. [26 refs.]

CUSHING and PATTON [this *Bulletin*, Vol. 31, p. 359], writing on "the Screw-Worm Fly of the New World," showed that this well-known cause of myiasis in man and animals had been wrongly identified as *Cochliomyia macellaria* and, believing the species to be then undescribed, they proposed to term it *C. americana*. This designation, however, as pointed out by the reviewer, is synonymous with *C. (Lucilia) hominivorax*, Coq., which dates from 1858 and, in default of proof of any earlier title, must be accepted as the true name of the Screw-Worm Fly.

The present contribution, after dealing in some detail with "Systematics," discusses *C. hominivorax* under the headings "Biology," "Geographical Distribution" and "Pathology." It is probable that the fly, which is believed to be "specifically parasitic" in the larval stage, deposits from 150 to perhaps 300 eggs at one time. Its distribution, like that of the true, non-parasitic, saprophagous *C. macellaria*, extends from the southern United States, through Central America and the West Indies, to the Argentine. In the five years 1928 to 1932 there were treated in public hospitals in British Honduras, British Guiana and Trinidad (with Tobago) 179 cases of myiasis, the majority of which, though perhaps not all, were probably due to *C. hominivorax*. Fifteen of these cases ended fatally, giving a case mortality of 8 per cent.

E. E. Austen.

STEWART (M. A.) & BOYD (A. N.). **A New Treatment of Traumatic Dermal Myiasis.**—*Jl. Amer. Med. Assoc.* 1934. Aug. 11. Vol. 103. No. 6. p. 402.

Traumatic dermal myiasis is defined as the invasion of wounds or skin ulcers by dipterous larvae. For treatment is advised chloroform in light vegetable oil.

The usual treatment for this condition in U.S.A. is irrigation with 20 per cent. chloroform in sweet cow's milk. This has to be made up fresh on each occasion and two to four treatments are usually needed. The authors find that light vegetable oil is a more satisfactory vehicle or diluent of the chloroform, for in this chloroform is entirely soluble.

If in a closed container the solution will keep indefinitely and the oil has a soothing effect on the wound : 15 per cent. of chloroform is a sufficient proportion. Seventeen cases were treated either by submersion for 30 minutes or by constant irrigation or keeping a flat gauze dressing saturated for the same period. In each case all the larvae were removed in a single treatment. In 13 of these, flies raised from the maggots were *Cochliomyia macellaria* Fabr. [See above.] A. G. B.

VON SZENTKIRÁLYI (Siegmond). Ueber eine durch Goldaugenlarven verursachte Hautveränderung. [A Skin Reaction caused by Lacewing-Fly Larvae.]—*Dermat. Woch.* 1934. Nov. 17. Vol. 99. No. 46. pp. 1502-1504. With 2 figs.

On two occasions in July 1934, in his garden in Hungary, the author was bitten by a lacewing-fly (*Chrysopa*) larva, once on the back of the hand and once on the arm. The bites resulted in a string of small, tense, red, itching vesicles, which persisted for four or five days and disappeared without treatment. Similar cases were repeatedly seen by the author in the course of practice, and he is convinced that they are not uncommon in June and July, when children playing in gardens are especially liable to be bitten, although the results are usually ascribed to ants or mosquitoes. Lacewing-fly larvae feed on the juices of aphids, but do not suck vertebrate blood ; the punctures occasionally made by their sucking-spears in human skin would seem to be experimental. [Similarly robber-flies (Asilidae), normally predators of other insects, have been known to inflict bites on man.] E. E. Austen.

YATSENKO (F.), PARETSKAYA (M.) & KIPRITCH (S.). [A Case of Myiasis of the Urethra.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 4. [In Russian p. 348.]

The authors report a case of a boy, 6 years old, passing maggots in his urine, some of which were actually seen protruding from the urethra. The larvae were identified as belonging to *Musca domestica*.

C. A. Hoare.

EVANS (A. C.). Studies on the Influence of the Environment on the Sheep Blow-Fly *Lucilia sericata* Meig. I. The Influence of Humidity and Temperature on the Egg.—*Parasitology.* 1934. Aug. Vol. 26. No. 3. pp. 366-377. With 8 figs. [11 refs.]

Lucilia sericata has a very wide distribution in temperate and sub-temperate countries, and in many parts of its range it causes myiasis of sheep. What climatic factors limit its distribution and abundance ?

The paper is the first of a series of articles in which the author proposes to discuss the effect of climatic factors upon successive stages of *Lucilia sericata*. The principal value of the paper is, therefore, to veterinary entomologists, though the author's conclusions may be briefly mentioned here. He finds that drier air retards the development of the egg, and that this effect is due to loss of water. The process is irreversible, and the egg cannot absorb moisture from a saturated atmosphere nor if it is covered with water. The author has also mapped those combinations of temperature and humidity which are fatal or favourable to the egg. P. A. Buxton.

STEWART (M. A.). *The Role of Lucilia sericata* Meig. Larvae in Osteomyelitis Wounds.—*Ann. Trop. Med. & Parasit.* 1934. Dec. 20. Vol. 28. No. 4. pp. 445-460. [23 refs.]

A number of factors are responsible for the beneficial action of maggots in the treatment of osteomyelitis. The maggots must be used with care because, though preferring necrotic tissue, they will attack healthy tissues.

All observers are agreed upon the beneficial effect of larvae of *Lucilia sericata* and other blow-flies in chronic osteomyelitis. The author discusses the vexed question of the nature of this action. From his own observations and those of others he concludes that many factors are at work. By means of their lacerating mouth-hooks and excreted trypsinase, they destroy and ingest necrotic tissue; most of the ingested bacteria are killed in the acid region of their mid-intestine which has a pH of 3.0-3.5; the wound is rendered alkaline by ammonia and calcium carbonate excreted by the larvae; the calcium ions are believed to stimulate phagocytosis, and perhaps both the calcium and the alkalinity promote the growth of healthy granulation tissue; and, finally, the bacterial exotoxin is thought to be rendered inert by the acidity in the mid-intestine of the larva. No bacteriophage has been found in the maggots. Experiments on guineapigs showed that all races of *L. sericata* investigated can establish themselves in and destroy healthy tissue; though given the choice they usually settle in wounds containing dead matter. The destruction of living tissues has been observed also in clinical cases; and the author showed in experiments on himself that the maggots can penetrate the healthy skin of the arm. For therapeutic purposes they must, therefore, be used with care if a destructive myiasis is to be avoided. *V. B. Wigglesworth.*

DUNN (Lawrence H.). *Prevalence and Importance of the Tropical Warble Fly, Dermatobia hominis* Linn., in Panama.—*Jl. Parasitology.* 1934. June. Vol. 20. No. 4. pp. 219-226.

In Panama, subcutaneous myiasis in man caused by the "gusano de monte," i.e., the larvae of *D. hominis* (this *Bulletin* Vol. 31, p. 63), has been recognized for eighty years at least, but has doubtless existed for centuries, albeit the Report of the Governor of the Panama Canal for 1928 speaks of two separate introductions of the maggot, in cattle from Venezuela and from Nicaragua. Surveying expeditions which preceded the construction of the Canal suffered severely from this form of myiasis, which is prevalent in the humid and low-lying as also in the forested regions of Panama, and from which no area of the body, whether clothed or not, from the eyelids to the middle of the back, is apparently exempt. In children the head and neck seem to be affected more often than other regions, and at least one case (in an infant 1½ years old) of the penetration of a larva of *D. hominis* through the anterior fontanelle into the brain, with fatal results, is on record. From personal experience, summarized previously (*loc. cit.*), the author considers the newly-hatched larva capable of penetrating drill clothing; but, difficult as it doubtless often is to explain the presence of the maggot in a particular spot, its capacity to pass through an unbroken, closely woven fabric needs to be demonstrated.

While a white man may harbour several of these parasites at the same time, and a native, although in no way immune, usually a

smaller number, cattle are much more severely attacked, sometimes to the extent of having "thousands of the warbles in their skin." In 1928, among cattle belonging to the Supply Department of the Canal, 900 head are said to have died and some 3,000 more to have been rendered unfit for slaughter as a result of the prevalence of warbles. Similar losses, though on a smaller scale, occurred in the following year, and in consequence the system of pasturing cattle in the Canal Zone was to a large extent abandoned.

In addition to human beings and cattle, the victims of *D. hominis* include sheep, dogs, cats, rabbits, and various species of wild animals, such as monkeys and agoutis (*Dasyprocta*).

[With so extensive a list of hosts, the abundance of this insect in Panama and other parts of Tropical America, and the frequency with which it parasitizes man are not surprising. Control would seem to be out of the question, and repellents (in this case against various species of Diptera forced by Dermatobia to act as porters for its eggs) have but a limited and temporary value in hot countries.] E. E. Austen.

i. MELENEY (Henry E.) & HARWOOD (Paul D.). **Human Intestinal Myiasis due to the Larvae of the Soldier Fly, *Hermetia illucens* Linné (Diptera, Stratiomyidae).**—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 45-49. With 2 figs.

ii. SCHWETZ (J.). Sur un cas de myiase intestinale provoquée par les larves de *Chrysomya putoria*, Wied. [**Intestinal Myiasis caused by Larvae of *Chrysomya putoria*.**]—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 469-471.

i. In October, 1933, some fifty larvae of *Hermetia illucens*, a fly which breeds normally in decaying vegetable and animal matter, and occurs in North and South America as also in Samoa, were passed at Nashville, Tennessee, by a white boy aged ten. Before expulsion, the larvae "caused symptoms of local irritation in the stomach and rectum, and spells of fainting," and their presence in the patient's intestine is presumed to have been a result of "eating raw fruit or vegetables on which the eggs of the fly had been deposited." Only one similar case of parasitization by larvae of *H. illucens* is believed to be on record. [Should the present instance find its way into text books, it is to be hoped that the spurious vernacular name "soldier fly," which, if used at all, can only be applied to the entire family Stratiomyidae, will be omitted.]

ii. More than one hundred larvae of *C. putoria*, nearly all in very young stages, were passed at stool by a European in Stanleyville, Belgian Congo. There were no morbid symptoms, and, although evidence is lacking, the infestation was probably acquired with food. Six of the larvae were reared, and PATTON, who determined the species, states that he has "never heard of this fly from intestinal myiasis before." [This widely distributed tropical African species—a "green-bottle" fly some 9 mm. in length—usually breeds in carrion, cow-dung and latrines. Its larvae in at least one instance (at Lorenzo Marques) have been found in sores.] E. E. A.

BOUVIER (G.) & VAN SLYPE (W.). Pseudo-myiase rampante. [**Creeping Pseudo-Myiasis.**]—*Ann. Soc. Belge de Méd. Trop.* 1934. Dec. 31. Vol. 14. No. 4. pp. 409-411.

A case with linear lesions on the foot with much itching; subcutaneous tunnels with vesicles; cause not found. Condition considered to be the

same as the larbisch of Senegal and other parts of the West Coast, but hitherto not recorded from Belgian Congo [see this *Bulletin*, Vol. 29, p. 277.] A. G. B.

JANISCH (Ernst). Ueber die Vermehrung der Bettwanze *Cimex lectularius* in verschiedenen Temperaturen. (Beobachtungen bei der Aufzucht von Bettwanzen II.). [**Multiplication of *C. lectularius* at Various Temperatures.**]—*Ztschr. f. Parasitenk.* 1935. Mar. 21. Vol. 7. No. 4. pp. 408-439. With 18 figs. [10 refs.]

The author gives a large mass of numerical fact relating to the reproduction and death of bedbugs (*Cimex lectularius*) kept under a variety of conditions of temperature, feeding, etc. Such information as this is valuable because it produces a better understanding of the growth of bug populations.

The author's general method was to isolate pairs of adults at a standard humidity of 75 per cent. and a number of different temperatures. Eggs and deaths were booked daily, also the hatching of eggs and the growth of larvae. Among a number of different subjects to which attention was given, the author studied the effect of the increasing age of the female on her powers of reproduction: towards the end of life a high proportion of the eggs which were laid failed to develop. He also exposed larvae to rather high temperatures, and investigated the effect of this upon the reproductive powers of the adult insect later in life. The author also studied the effect of keeping bugs continuously at 34°C.; at this temperature several generations follow one another, but the insect eventually dies out. The following figures, extracted from many others, are surely interesting:—

27°C.	mean no. of eggs	318, 293	viable.
32	"	119, 88	"
34	"	88, 67	"

These facts are consistent with the observations of MELLANBY, quoted below, who shows that 34°C. is the highest temperature at which eggs can develop if the exposure is continuous.

We are grateful to the author for showing how inconsistent the results are if different individual insects are treated in a way which is believed to be identical. But many of the experiments are presented almost in the original form so that it is difficult to grasp what conclusion may justly be drawn from them. No tests of significance in the statistical sense appear to have been applied, so that one cannot always distinguish the results which may justly be attributed to the experimental conditions from those which are due to the inherent variability of the insect. P. A. Buxton.

MELLANBY (Kenneth). **A Comparison of the Physiology of the Two Species of Bed-Bug which attack Man.**—*Parasitology*. 1935. Feb. Vol. 27. No. 1. pp. 111-122. With 3 figs. (1 map.)

The author endeavours to discover by controlled laboratory experiments why it is that two species of bedbug so similar in shape and size inhabit two rather different climatic zones. Is it possible to discover whether the tropical species tolerates a higher temperature or breeds more rapidly at higher temperatures than the species found in temperate countries?

The author confines himself to the study of temperature and humidity over a very wide range of conditions. He finds that humidity has very

little effect on bugs provided they are fed sufficiently frequently: the drier the air the more rapidly they lose water, but they can make up the loss at their next meal. But starving bugs live much longer in moist than in dry air. The two species are similar in this respect, and in the rate at which they lose water into atmospheres of different relative humidities. As to the upper temperature limit, it is identical for the two species, the lowest temperature which kills all bugs on an hour's exposure being 44°C. and on a 24 hours' exposure 40°C. The limit for eggs is 1° higher for both species. But at the lower end of the temperature scale there is a significant difference between the species, for the developmental zero for the egg of *Cimex lectularius* is 13°C., for *rotundatus* 15°C. It was also found that at temperatures below 30°C. the egg of *lectularius* develops more rapidly and the larva also becomes adult more rapidly, so that this species is the more efficient multiplier at those temperatures. Above 30°C. there is very little difference between the two species.

The author then passes on to consider the geographical distribution of the two bugs, and finds that *C. rotundatus* is confined to a belt which only extends outside the geographical tropics in a few places. *C. lectularius*, on the other hand, is very widely distributed in the temperate zones, passing within the Arctic circle in Scandinavia. But within the tropics it has become established in a number of places, where it seems able to exist just as well as the tropical bug. It seems, therefore, that there is a good fit between the facts of geographical distribution and the results of laboratory experiments. P. A. B.

OHMORI (N.). **Experimental Studies on the Influence of Low Temperatures upon the Tropical Bed-Bug (*Cimex hemipterus* Fabricius).** First Report.—*Taiwan Igakkai Zasshi* (Jl. Med. Assoc. Formosa). 1934. Oct. Vol. 33. No. 10 (355). [In Japanese pp. 1511-1527. With 2 charts. [9] refs.] English summary pp. 139-140.]

The paper describes the distribution of the tropical bedbug in Formosa, Japan and Korea, and endeavours to explain it by considering winter temperature as a possible limiting factor.

It has been observed that the tropical bedbug, *Cimex hemipterus*, is common in Formosa, which has a tropical climate. It cannot be found in Japan, and this might be attributed to low winter temperature acting as a limiting factor. But the occurrence of the insect in Korea is not easy to explain at first sight.

The author's experiments show that eggs of this insect can live without developing for many weeks at 9°C. If such eggs are subsequently removed to 15°C., they develop and hatch. The larvae are capable of moulting at 10°C. but not at 9°C., the adults and larvae living many weeks at these temperatures. The view is expressed that such observations as these explain the absence of the insect from Japan, where the houses are only very slightly heated in winter; it can exist in Korea because the domestic heating is more thorough though the winter temperatures are low. [The interest of the work would be increased if the author could give facts about the temperature in houses of different types at different times of year, comparing his observations with shade temperature outside.] P. A. B.

AFRICA (Candido M.). Three Cases of Poisonous Insect Bite Involving *Triatoma rubrofasciata*.—*Philippine Jl. Sci.* 1934, Feb. Vol. 53. No. 2. pp. 169-177. With 1 plate.

The author describes the clinical symptoms observed in three patients in the Philippines who appear to have been bitten by the Reduviid bug, *Triatoma rubrofasciata*.

Each patient was seen by a medical man, and full clinical notes are published. Briefly, they suffered from local pain and itching, followed by widespread numbness, rigors and oedema of several parts distant from the bite. This was followed by rapid recovery. In each instance the patient secured an example of this bug and was convinced that that was the cause of the trouble; the possibility remains that some error in identification took place, for such cases of poisoning are surprisingly rare in view of the insect's very wide distribution and abundance in many parts of the Oriental region. Moreover, as the author points out, several writers have experienced the bite and found that the effect was negligible. The author suggests that the grave symptoms may be caused by the injection of saliva into a blood vessel rather than into subcutaneous tissues; it should not be difficult to put this to experimental proof.

P. A. B.

FROES (Heitor P.). Dermatite à coléoptères vésicants. Nouvelles expériences et observations sur les léoptères vésicants du genre *Paederus* (Staphylinidae). [*Beetle Dermatitis*.]—*Arch. Ital. Sci. Med. Colon.* 1934. July 1. Vol. 15. No. 7. pp. 481-488. With 2 figs. English summary (4 lines).

The author's experiments were made in Brazil with a species of *Paederus* determined to be *P. brasiliensis*. They are detailed at some length and showed that the blistering fluid occurs throughout the body of the beetle and is extruded only when the creature is crushed or pressed strongly against the skin.

A. G. B.

HINMAN (E. Harold) & KAMPMEIER (R. H.). Intestinal Acariasis due to *Tyroglyphus longior* Gervais.—*Amer. Jl. Trop. Med.* 1934. July. Vol. 14. No. 4. pp. 355-362. With 1 fig. [13 refs.]

The authors give an account of mite infestations in man which have caused either a rash, or urinary symptoms, or diarrhoea. They describe briefly two cases of infestation with *Tyroglyphus longior*, in one of which there was diarrhoea and the proctoscope revealed minute scattered ulcers, negative for amoebae. Looseness of the bowel had been recurrent in this man. Treatment was withheld and after six days the mites disappeared and the stools became formed. This patient died of pneumonia and there was found congestion of the mucosa of the large gut with numerous small ulcers.

In experiments to determine whether *T. longior* fed to dogs would produce diarrhoea they failed to do so. Following HASE the authors question whether the intestinal disturbance is an allergic reaction or is due to toxins liberated from the mites; they suggest that the spines on these arthropods might injure the villi.

[According to MÖNNIG (Veterinary Helminthology and Entomology: Baillière, Tindall & Cox, 1934)—

“Höve and Fiedler report several cases of sudden deaths in horses and pigs which showed at autopsy a slight enteritis, and the presence

of the meal-mite *Aleurobius farinae*, in scrapings of the intestinal mucosa. No other explanation for the deaths of the animals could be found. The mites were also present in the grain supply from which the animals had been fed." A. G. B.

DAVIES (J. Rodyn). [The "Chigoe Flea."] [Correspondence.]—*East African Med. Jl.* 1935. Feb. Vol. 11. No. 11. p. 367.

With reference to the introduction of the chigoe flea to Abyssinia which NEGELSBACH assigns to a date between 1920 and 1924 [see this *Bulletin*, Vol. 31, p. 735] Davies writes that about the period 1924–26 the natives in S. Abyssinia called the insect Moyale, associating this place with its first appearance. He suggests that Moyale was reached via Marsabit and Meru and that the chigoe reached Abyssinia by way of the Northern Frontier Province of Kenya.

A. G. B.

LOW (G. Carmichael) & CORDINER (G. R. Mather). **A Case of Porocephalus Infection in a West African Negro.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 535–537. With 1 plate.

Infections with the cysts of *Porocephalus armillatus* have been described from Tropical Africa [see Vol. 1 of this *Bulletin*, p. 405]. They have in every case been found post-mortem. Here they were shown up by X-rays in a negro in London as "calcified opacities" in the liver and other parts of the abdomen. Some of these shadows showed clearly the curved or spiral appearance taken up by the nymphal forms within the cyst.

A. G. B.

PAVLOVSKY (E. N.) & STEIN (A. K.). [The Action of *Scolopendra Venom upon Human Skin. II.*]—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1–2. [In Russian pp. 88–90.]

Working in the Crimea, the authors carried out 20 experiments upon the effect of the venom of *Scolopendra cingulata* upon human skin. The isolated poison glands of several score myriapods were dried, emulsified in saline, and left to stand overnight, after which the clear fluid was injected intradermally. The injection provokes an acute local inflammatory reaction which increases up to the fourth or fifth hour after the inoculation, and is characterized by acute pain, oedema and the formation of a papule. The latter may persist up to four days, after which it is absorbed. The reaction observed under experimental conditions is similar to that produced by the bite of the myriapod. The drying of the glands does not effect the toxic properties of the venom which are retained for more than 15 months.

C. A. Hoare.

i. KELLAWAY (C. H.). **A Note on the Venom of the Sydney Funnel-Web Spider, *Atrax robustus*.**—*Med. Jl. Australia.* 1934. May 26. 21st Year. Vol. 1. No. 21. pp. 678–679.

ii. MACKERRAS (I. M.). **The Venom of *Atrax robustus*** Cambridge. [Correspondence.]—*Ibid.* June 16. No. 24. p. 794.

i. The author finds that though the bite of *Atrax robustus* is deadly to man, four fatalities being recorded and several instances of extremely

severe symptoms, he was unable to produce symptoms in rabbits, guineapigs or mice which were bitten or injected with venom. The spiders were six fine specimens, kept in captivity. The experimental animals, he suggests, may have been immune to the venom, or the venom was reduced in potency, or the symptoms in man are due to acute anaphylactic shock in sensitive individuals, or are due to a potent bacteria-produced toxin not invariably present in the venom; he is inclined towards the first of these hypotheses.

ii. In an interesting letter the writer says that in his own experiments with this species three guineapigs were bitten. Two showed no ill-effects and one died, but it was in an enfeebled state.

A. G. B.

MARZINOVSKY (E.). [The Clinical Aspects of *Lathrodictes Bite*.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 4. [In Russian pp. 342–348. With 5 figs.]

A detailed account is given of the clinical course of three cases of persons bitten by the Karakurt spider, *Latrodectus tredecimguttatus*.

These cases were selected from a large number observed in Turkestan the general symptoms of which are as follows: At the site of the bite there appears a haemorrhagic spot or isolated petechiae and a slight swelling of the skin. There is acute local pain radiating into the adjoining areas, general weakness, copious sweating, and tremor in the legs, the patient being unable to stand. The pulse-rate is slow, respiration irregular, the temperature is slightly raised, there is insomnia, pains in the region of the solar plexus, marked *défense musculaire*, anuria and constipation. As regards the blood-picture, there is slight leucocytosis at the beginning (9,400) and about 5 per cent. of eosinophils by the third day. The symptoms persist from three to five days.

C. A. Hoare.

GILBERT (Elmer W.) & STEWART (Charles M.). **Effective Treatment of Arachnidism by Calcium Salts. A Preliminary Report.**—*Amer. Jl. Med. Sci.* 1935. Apr. Vol. 189. No. 4. pp. 532–536. [29 refs.]

The authors publish five cases of *Latrodectus mactans* bite in which the intense pain was promptly relieved by injection of calcium salts.

It is generally accepted, they say, that the venom directly stimulates the myoneural junctions or that it acts on the nerve-endings; since calcium depresses the neuromuscular junctions, salts of this metal were selected for trial. Intravenous injection of 10 per cent. CaCl_2 were found to give instantaneous and prolonged relief of pain, and to produce immediate relaxation of muscle spasm, but owing to its necrotic action on tissue outside a vein calcium gluconate (10 cc. of 10 per cent. sol.) was substituted, with complete success. The intramuscular route is preferable for children. The case records bear out the authors' statements.

A. G. B.

UGANDA PROTECTORATE ANNUAL MEDICAL AND SANITARY REPORT FOR THE YEAR ENDED 31st DECEMBER, 1933. Appendix I. pp. 57–59.—**Annual Report of the Government Entomologist for 1933.**

In Uganda, the two most dangerous species of *Anopheles* are *A. gambiae* and *A. funestus*, whose pre-adult life-cycles, in approximately

natural conditions, were found to vary in length from 11 to 16 days in the case of the former, and from 20 to 21 days (two experiments only) in that of the latter. No mosquitoes were observed to breed in an unshaded gutter, an experiment which was continued. In shaded gutters *Aedes aegypti* bred freely, but no Anopheline larvae were met with.

As regards fleas, it is considered that, at least locally in rural Buganda, *Xenopsylla brasiliensis*, as in certain districts in Kenya, is the chief carrier of plague; and that the range of *X. cheopis*, which in Kampala is the more abundant species, is very restricted.

In West Nile, *Glossina palpalis* was found to be moderately abundant along the River Ora, and also in places on the Nile itself; and both *G. pallidipes* and *G. morsitans* were locally common. For the protection of the population, which is living in close contact with *G. palpalis*, a limited amount of clearing on the Ora was thought advisable. In view of the scarcity of fly along part of the shore of Lake Edward and in the Katwe Forest, whence the neighbouring people originally derived their food, restricted advance into the damper portion of the Forest was recommended. On the other hand the "damp forested ravines" in Katwe, which yield hut-poles, but all of which are to some extent infested with fly, should remain closed. In the course of a brief survey of the Kagera River, within the confines of Uganda, *G. palpalis* was not found.

Regarding the prevalence at certain seasons of *Simulium damnosum* near Jinja it is interesting to learn that preliminary attempts at trapping this pestilent little fly have proved encouraging, and that the experiments, especially as to the lure of scent in this connexion, are to be continued [see this *Bulletin*, Vol. 31, p. 60]. E. E. A.

CAMINOPETROS (J.). Addition à la liste des phlébotomes signalés pour la première fois en Grèce.—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 44-46.

CURRAN (Jean A.), CONNERY (Joseph E.) & GOLDWATER (Leonard J.). A Study of Intestinal Parasitism in New York City.—*Jl. Parasitology.* 1935. Apr. Vol. 21. No. 2. pp. 126-127.

DUNN (Lawrence H.). Notes on the Water Lettuce, *Pistia stratiotes* Linn., as a Nursery of Insect Life.—Reprinted from *Ecology.* 1934. July. Vol. 15. No. 3. pp. 329-331.

HERMS (W. B.). Mosquito Control in California under the CWA.—*Jl. Econom. Entom.* 1934. Oct. Vol. 27. No. 5. pp. 1014-1029. With 3 figs.

HULSHOFF (A. A.) & FLU (P. C.). A Case of Melioidosis.—*Acta Leidensia (Scholae Med. Tropicae).* 1934. Vol. 9. pp. 162-178. With 5 figs. on 1 plate. [See this *Bulletin*, Vol. 31, p. 344.]

IMPALLOMENI (Rosario). Il parassitismo intestinale in Cirenaica.—*Giorn. Ital. di Malat. Esot. e Trop.* 1935. May 31. Vol. 8. No. 5. pp. 114, 117-20. [15 refs.]

IOFF (I.) & ARGYROPULO (A.). Die Flöhe Armeniens.—*Ztschr. f. Parasitenk.* 1934. Dec. 11. Vol. 7. No. 2. pp. 138-166. With 21 figs.

DE MAGALHÃES (Octavio). Hemiplegias organicas provocadas pelos venenos ophidico e escorpionico.—*Rev. Med.-Cirurg. do Brasil.* 1935. Apr. Vol. 43. No. 4. pp. 113-118. With 1 fig.

NIÑO (Flavio I.) & TRIACA (José Abel). Miasis forunculosa por larvas posiblemente de "*Cochliomya macellaria*."—*Bol. Inst. Clin. Quirúrg.* 1934. Vol. 10. Nos. 84-87. pp. 201-204. With 5 figs.

- DE PAULA E SILVA (G. S.). Balantidiosis intestinal. Tratamiento por la dieta de Greene-Scully.—*Arch. Argentinos Enferm. Aparato Digest. y Nutric.* Buenos Aires. 1934. Aug.-Sept. Vol. 9. No. 6. pp. 551-562. With 3 charts. [12 refs.]
- PIEKARSKI (Gerhard). Eine einfache Vorrichtung zur Fütterung blutsaugender Arthropoden an Warmblütlern.—*Zent. f. Bakt.* I. Abt. Orig. 1935. Mar. 18. Vol. 133. No. 7/8. pp. 470-471. With 2 figs.
- ROY (D. N.). Dental Myiasis.—*Indian Med. Gaz.* 1934. Sept. Vol. 69. No. 9. p. 500.
- RUSSELL (Paul F.). Biological and Medical Research at the Bureau of Science, Manila.—*Quarterly Rev. Biol.* 1935. June. Vol. 10. No. 2. pp. 119-153. [478 refs.]
- STREEF (G. M.). De waterstofionenconcentratie van het bloed bij Europeanen in gematigde lichtstreken in vergelijking met die bij bewoners der tropen.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Apr. 2. Vol. 75. No. 7. pp. 559-563. English summary (10 lines).
- SUAREZ (Ramon M.) & COSTA MANDRY (O.). Estudios hematologicos de algunas enfermedades tropicales ; su comparacion con casos normales, con utilizacion del hematocrito de Wintrobe.—*Bol. Asoc. Med. de Puerto Rico.* 1935. Feb. Vol. 27. No. 2. pp. 27-44. [12 refs.]
- TAYLOR (F. H.). Medical Entomology in Australia.—*Health.* Canberra. 1934. Nov. Vol. 12. No. 11. pp. 88-91.
- TREILLARD (M.). *Myzomyia minima* Theobald, doit-elle être appelée *Myzomyia vincenti* Laveran ?—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 750-751.
- URECHIA (C. I.) & DRAGOMIR (L.). Névralgie du petit sciatique et du sciatique après une injection de quinine.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1935 June 10 51st Year 3rd Ser. No. 19. pp. 951-953. With 1 fig.
- YAKIMOFF (V.) & SOKOLOV (B.). On a New Coccidium, *Eimeria beckeri* n. sp., of the Ground-Squirrel, *Citellus pygmaeus* Pall.—*Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 4. [In Russian pp. 331-334. With 2 figs. English summary p. 334]
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REVIEWS AND NOTICES.

PEIPING UNION MEDICAL COLLEGE. **Laboratory Manual of the Department of Bacteriology and Immunology.** Prepared under the Direction of C. E. LIM. Second Edition.—190 pp. With 3 figs. 1935. Peiping, China. [\$1.50.]

The second edition of this little book, the first edition of which was reviewed in the *Tropical Diseases Bulletin*, Vol. 26, p. 867, hardly calls for any detailed comment. Some changes have been made and certain new matter has been introduced, but on the whole the new edition is very much like the previous one. The book still remains a guide to the various techniques employed in the Department of Bacteriology and Immunology of the Peiping Union Medical College, N. China, and is thus intended chiefly for local use. It gives the composition of the various media, solutions and stains used and the methods of carrying out the various reactions and tests which are undertaken in this department. The section devoted to the care and breeding of laboratory animals still remains a feature of the book, while additional information regarding the methods of examination for pathogenic fungi is given. As did the first edition, the new one deals with bacteriological and serological matters, the methods of blood examination and protozoal diagnosis being omitted. As a handy work of reference, though written for one particular laboratory in China, the book should prove very useful in any bacteriological department.

C. M. Wenyon.

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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1935.

[No. 10.]

SLEEPING SICKNESS.

ECONOMIC ADVISORY COUNCIL. **East Africa Sub-Committee of the Tsetse Fly Committee** [HEMMING (Francis), Chairman]. **Report.** Cmd. 4951.—56 pp. 1935. London: H.M.S.O. [1s.]

In May, 1934, the Secretary of State for the Colonies communicated to the Economic Advisory Council the report of the Conference on Tsetse and Trypanosomiasis Research held at Entebbe in 1933, and also the conclusions of the recent Governors' Conference on the same subject, and asked that he might be furnished with the observations of the Council's Tsetse Fly Committee on these papers. On 3rd July, 1934, the Earl of Plymouth, Chairman of the Tsetse Fly Committee, appointed an East Africa Sub-Committee of that Committee to prepare a report on these questions.*

In the introduction to their Report the Sub-Committee state that one of the most important subjects they have had to consider was the question of the future of the Human Trypanosomiasis Institute, Entebbe. They received valuable assistance in this part of their inquiry from Dr. DUKE and from Dr. KAUNTZE, Director of Medical Services, Uganda. In addition they are much indebted to Dr. Edward MELLANBY, Secretary, Medical Research Council, for the assistance which he gave in regard to the co-operation which might be obtained from the Medical Research Council in carrying out certain investigations suggested by the Conference.

The Sub-Committee state that they found it convenient to preface their discussion with a general outline of the problem as a whole, and consequently in Section II of the Report they describe briefly the main characteristics of trypanosomiasis, both animal and human, and the principal methods available for controlling it. Section III is devoted to a discussion of items of fundamental research, the object of which is to obtain further knowledge of the causes of the disease; and Section IV emphasizes the necessity for maintaining contact between the scientific work on these subjects being carried out in different parts of Africa and the world. Section V consists of a summary of the principal conclusions and recommendations of the Sub-Committee.

* The members of the Sub-Committee were:—

Mr. Francis Hemming, Chairman; Dr. W. Horner Andrews; Sir Arthur Bagshawe; Sir Guy Marshall; Sir Thomas Stanton; Dr. C. M. Wenyon; Mr. F. G. Lee; Mr. D. H. F. Rickett, Secretary.

SECTION II. THE CONTROL OF TRYPANOSOMIASIS IN MAN AND ANIMALS.—After giving an excellent and readily understandable statement of the "General Character of the Problem" the report passes to a consideration of the various available methods of control. These are of three kinds:—

i. *Control by administrative measures.*—Broadly these represent an attempt to prevent or eradicate infection by controlling the movements of population. There seems little doubt that the spread of sleeping sickness has been largely assisted, if not caused, by the development of the means of communication which took place at the end of last century. Obviously infected persons should not be at liberty to migrate where they please, fishing in fly-infested areas should not be permitted except under control, and access to watering places similarly endangered should only be allowed after clearing of the bush. Such measures as these may be regarded as part of the routine to be observed in preventing the spread of infection. Administrative control in the wider sense has, however, a larger scope than this. The policy of controlling population movements has in most cases been designed to play a large part in furnishing a solution of the sleeping sickness problem. The most drastic and most obvious of these measures is the evacuation of the population from an area affected by an outbreak of sleeping sickness. Reference is made to the evacuation in Uganda and the benefit which it was anticipated would accrue therefrom. Subsequent discoveries have shown, however, that there is little prospect of success for such a policy, if unaccompanied by direct attempts to exterminate the fly. Experience has shown that temporary withdrawals of the population would often in practice tend to become permanent. Apart from the grave effects upon the industry of the areas concerned, the absence of population promotes the growth of bush and multiplication and spread of game; and usually these factors operate together to assist the advance of fly. Undoubtedly the most effective means of preventing the spread of fly is by the concentration into closer settlements of scattered native populations. It has been found that a settlement with a minimum population of 3,500 to 4,000 is large enough to secure freedom from fly roughly two years from its establishment. The Entebbe Conference considered this method of control very carefully and agreed that organized settlement and development of this nature was ordinarily the most important general preventive measure which could be taken by administrations in the campaign against trypanosomiasis, and this view is fully shared by the Sub-Committee.

ii. *The control of tsetse flies.*—This section of the report is in large measure devoted to an account of the results and progress of the work proceeding in Tanganyika under the direction of SWYNNERTON. The biggest fly belt in Tanganyika is 500 miles at its longest by 300 miles at its widest point. In order to deal with a problem of this magnitude these great fly belts must be subdivided by means of suitable barriers into a number of small compartments from which the fly cannot escape. At the present time the great Shinyanga fly-belt has been divided up by corridor clearings into a number of blocks in which different methods of eradicating tsetse are being tested, e.g. (1) organized grass fires, (2) differential, as opposed to wholesale, clearing, (3) fly and game barriers formed by dense strips of thicket, (4) fly traps, and (5) eradication of the fly by protecting blocks of bush from grass fires. The advantages and limitations of these various measures are discussed in some detail.

iii. *The control of trypanosomiasis by chemotherapy.*—The third of the principal methods of control is the treatment of the disease by drugs. It has been shown by a number of clinical trials that "Bayer 205" has a definite prophylactic value, but the sub-committee agree with the Entebbe Conference that further information is required before the drug can be employed to the fullest effect in this direction. There is little doubt that "Bayer 205" remains in the blood and tissues for a considerable time, probably for several months, and that it is eliminated in the urine very slowly. Very little work has, however, been done on the rapidity or manner of excretion of the drug from the animal body. The Entebbe Conference recommended "that the Medical Research Council should be approached with a request to work on this problem" and they suggested that the subject might be of interest to Dr. WORMALL, who is engaged on cognate research under the auspices of the Medical Research Council. In order to give consideration to this suggestion, the sub-committee invited the Secretary of the Medical Research Council to attend one of its meetings and discuss the matter with them. Dr. MELLANBY informed the sub-committee that Dr. WORMALL had expressed his willingness to undertake preliminary investigations on the problem in question. WORMALL proposed to study the methods of STEPPUHN and UTKINA-LYUBOWZEWA (1924) and of LANG (1931) for the chemical determination of "Bayer 205" and then to examine the excretion of the drug by small animals after one or more injections.

At the same meeting the sub-committee discussed with Dr. MELLANBY the recommendation put forward by the Entebbe Conference that the Medical Research Council should be approached with a view to interesting prominent British research workers in the synthesis of therapeutic compounds for the treatment of trypanosomiasis. The suggestion of the Conference was that such drugs could then be tested in East Africa. From the discussion which the sub-committee had with Dr. DUKE and Dr. KAUNTZE they had gathered that it was the feeling of those engaged in work on trypanosomiasis in British Territories in Africa "that the drugs at present employed . . . are susceptible of improvement." The Conference was accordingly anxious to secure the co-operation of scientific workers in this country in the production for subsequent trial in Africa of new forms of drug for use against trypanosomiasis. Dr. MELLANBY assured the sub-committee that there is no lack of such new compounds awaiting experimental use in Africa. In 1927, the Medical Research Council, with the co-operation of the Department of Scientific and Industrial Research, appointed a Chemotherapy Committee with the main object of investigating drugs having specific action in trypanosomiasis and malaria. For some years before this, the Medical Research Council had already been supporting two groups of workers engaged in research for new trypanocidal drugs, viz., Professor COHEN at Leeds and Professor BROWNING at Glasgow, and Dr. KING and Miss DURHAM at Hampstead. The Chemotherapy Committee began by inviting a number of well-known chemists to prepare a series of new compounds for test on experimental trypanosomiasis lines which had been carefully discussed before. To deal with the new compounds, another Biological Station under the reviewer at the Liverpool School of Tropical Medicine was established by the Medical Research Council in addition to the two already so engaged. [It would be fairer to say that this centre was established, and is mainly financed, by the Liverpool School of Tropical Medicine,

and that it is supported by an annual grant from the Medical Research Council].

Dr. MELLANBY went on to inform the sub-committee that Professor MORGAN of Teddington had prepared a long series of compounds, which had been examined by Professor YORKE, and that five of these compounds had been selected as having maximal activity. Dr. KING of the National Institute for Medical Research had also discovered two arsenicals of novel type of extreme efficacy in trypanosomiasis of mice and rabbits. Dr. MELLANBY further informed the committee that having regard to the fact that there were now seven drugs which had been synthesized by workers under the Chemotherapy Committee known to have considerable trypanocidal activity, the Medical Research Council believed that the time had come when the best opportunities for the clinical trial of these drugs should be made available. The sub-committee considered the subject in the light of this information, and reached the conclusion that the importance of securing the most precise information possible in regard to the use of these new drugs is such that the appointment of a special investigator to undertake this work would be fully justified. They accordingly recommend that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests on trypanocidal drugs.

[The Secretary of the Medical Research Council was a little premature when he informed the Sub-Committee that the Chemotherapy Committee has available 7 drugs ripe for testing in the field. As a matter of fact, only one of these compounds—Preparation S.107 of Professor MORGAN—had been sufficiently examined to justify its despatch to Africa for testing in the field on cases of sleeping sickness. The other six compounds have not so far been administered to man, nothing is known about the dosage in which they could be used, and they have not even been prepared in more than minute amounts.]

SECTION III. PROTOZOAL RESEARCH.—This portion of the report summarizes the work which is being done at the Human Trypanosomiasis Institute, Entebbe, and also the investigations which have been conducted in other parts of Africa by CORSON and others during the last few years. All this work is familiar to readers of this *Bulletin*.

SECTION IV. CONTACTS WITH RESEARCH WORKERS IN OTHER COUNTRIES.—The main purpose of the Entebbe Conference was to co-ordinate the tsetse and trypanosomiasis research being done at the present time in East Africa. From their examination of the program of research drawn up by the Conference the sub-committee is convinced that that result has been in large measure attained. This important subject is discussed very fully in the report.

In the sub-committee's opinion, the publication of the *Tropical Diseases Bulletin* goes far towards filling the need for information felt by research workers in trypanosomiasis. In order that workers in the field should be informed of what is going on in different parts of Africa at the earliest possible moment, Sir Arthur BAGSHAW, Director of the Bureau, informed the sub-committee that he was prepared to arrange for the list of titles of papers awaiting review, which he compiled each week, to be reproduced in cyclostyle and distributed to the Directors of Medical Services at a small charge. The sub-committee believes that this will be of real service to those engaged on trypanosomiasis research in Africa.

SECTION V. SUMMARY OF PRINCIPAL CONCLUSIONS AND RECOMMENDATIONS.—In this very interesting and important section, the sub-committee first of all summarizes its principal conclusions and then lays down certain definite recommendations. It is unfortunately impossible to reproduce the whole of this section here, but the following are the chief recommendations.

i. *Control of trypanosomiasis in man and animals.*

(a) *Control by administrative measures.*—This calls for constant co-operation between the large number of departments concerned. Small *ad hoc* bodies might therefore with advantage be set up in the larger territories to secure an adequate machinery for consultation and discussion of problems as they arise. The proposal that a central body should be set up either in Africa or in the United Kingdom to conduct a general investigation into the principles to be adopted in applying administrative methods of control was not received with favour.

(b) *Control of tsetse flies.*—It is strongly recommended that the fullest financial support should be given to the Tsetse Research Department in the Tanganyika Territory. As there is a great danger that the Department may lose the services of officers who by training and past experience are exceptionally qualified for their work, it is recommended that the question of granting permanent pensionable status to the officers now working in the Department should receive consideration at the earliest possible moment. It is also recommended that the biological study of tsetse flies in *rhodesiense*, *gambiense* and *brucei* areas should be included in the program of research; and that the biological study of the stomach contents of the tsetse fly should be undertaken by Mr. C. B. SYMES at the Medical Laboratory, Nairobi.

(c) *The control of trypanosomiasis by chemotherapy.*—It is recommended that an investigation of the prophylactic value of Bayer 205 should be undertaken, and that the Secretary of State should invite the Medical Research Council to arrange preliminary investigations on the rapidity of the excretion of Bayer 205 to be carried out by Dr. WORMALL.

With the object of testing the new drugs prepared by the Chemotherapy Committee, it is suggested that the Secretary of State should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests on trypanocidal drugs and to arrange for him to be afforded all necessary facilities for his work, including the concentration in some suitable centre of a sufficient number of sleeping sickness cases who could be kept under observation.

It is also recommended that the Secretary of State for Dominion Affairs should ascertain from the Government of Southern Rhodesia whether it would be possible for the Trypanosomiasis Bureau to test the veterinary effects of some new drugs; and from the Government of South Africa whether these tests could also be undertaken at the Veterinary Research Institute, Onderstepoort.

ii. *Protozoological research.*—It is recommended that in order to enable Dr. DUKE to complete his present experiments, the Human Trypanosomiasis Institute, Entebbe, should be maintained on its present basis till the 31st Dec., 1935, when the Institute as such should be closed; and that thereafter the Medical Department in Uganda should undertake such research as its resources permit.

and that it is supported by an annual grant from the Medical Research Council].

Dr. MELLANBY went on to inform the sub-committee that Professor MORGAN of Teddington had prepared a long series of compounds, which had been examined by Professor YORKE, and that five of these compounds had been selected as having maximal activity. Dr. KING of the National Institute for Medical Research had also discovered two arsenicals of novel type of extreme efficacy in trypanosomiasis of mice and rabbits. Dr. MELLANBY further informed the committee that having regard to the fact that there were now seven drugs which had been synthesized by workers under the Chemotherapy Committee known to have considerable trypanocidal activity, the Medical Research Council believed that the time had come when the best opportunities for the clinical trial of these drugs should be made available. The sub-committee considered the subject in the light of this information, and reached the conclusion that the importance of securing the most precise information possible in regard to the use of these new drugs is such that the appointment of a special investigator to undertake this work would be fully justified. They accordingly recommend that the Secretary of State for the Colonies should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests on trypanocidal drugs.

[The Secretary of the Medical Research Council was a little premature when he informed the Sub-Committee that the Chemotherapy Committee has available 7 drugs ripe for testing in the field. As a matter of fact, only one of these compounds—Preparation S.107 of Professor MORGAN—had been sufficiently examined to justify its despatch to Africa for testing in the field on cases of sleeping sickness. The other six compounds have not so far been administered to man, nothing is known about the dosage in which they could be used, and they have not even been prepared in more than minute amounts.]

SECTION III. PROTOZOAL RESEARCH.—This portion of the report summarizes the work which is being done at the Human Trypanosomiasis Institute, Entebbe, and also the investigations which have been conducted in other parts of Africa by CORSON and others during the last few years. All this work is familiar to readers of this *Bulletin*.

SECTION IV. CONTACTS WITH RESEARCH WORKERS IN OTHER COUNTRIES.—The main purpose of the Entebbe Conference was to co-ordinate the tsetse and trypanosomiasis research being done at the present time in East Africa. From their examination of the program of research drawn up by the Conference the sub-committee is convinced that that result has been in large measure attained. This important subject is discussed very fully in the report.

In the sub-committee's opinion, the publication of the *Tropical Diseases Bulletin* goes far towards filling the need for information felt by research workers in trypanosomiasis. In order that workers in the field should be informed of what is going on in different parts of Africa at the earliest possible moment, Sir Arthur BAGSHAW, Director of the Bureau, informed the sub-committee that he was prepared to arrange for the list of titles of papers awaiting review, which he compiled each week, to be reproduced in cyclostyle and distributed to the Directors of Medical Services at a small charge. The sub-committee believes that this will be of real service to those engaged on trypanosomiasis research in Africa.

SECTION V. SUMMARY OF PRINCIPAL CONCLUSIONS AND RECOMMENDATIONS.—In this very interesting and important section, the sub-committee first of all summarizes its principal conclusions and then lays down certain definite recommendations. It is unfortunately impossible to reproduce the whole of this section here, but the following are the chief recommendations.

i. *Control of trypanosomiasis in man and animals.*

(a) *Control by administrative measures.*—This calls for constant co-operation between the large number of departments concerned. Small *ad hoc* bodies might therefore with advantage be set up in the larger territories to secure an adequate machinery for consultation and discussion of problems as they arise. The proposal that a central body should be set up either in Africa or in the United Kingdom to conduct a general investigation into the principles to be adopted in applying administrative methods of control was not received with favour.

(b) *Control of tsetse flies.*—It is strongly recommended that the fullest financial support should be given to the Tsetse Research Department in the Tanganyika Territory. As there is a great danger that the Department may lose the services of officers who by training and past experience are exceptionally qualified for their work, it is recommended that the question of granting permanent pensionable status to the officers now working in the Department should receive consideration at the earliest possible moment. It is also recommended that the biological study of tsetse flies in *rhodesiense*, *gambiense* and *brucei* areas should be included in the program of research; and that the biological study of the stomach contents of the tsetse fly should be undertaken by Mr. C. B. SYMES at the Medical Laboratory, Nairobi.

(c) *The control of trypanosomiasis by chemotherapy.*—It is recommended that an investigation of the prophylactic value of Bayer 205 should be undertaken, and that the Secretary of State should invite the Medical Research Council to arrange preliminary investigations on the rapidity of the excretion of Bayer 205 to be carried out by Dr. WORMALL.

With the object of testing the new drugs prepared by the Chemotherapy Committee, it is suggested that the Secretary of State should invite the Medical Research Council to arrange for an investigator to proceed to Africa for the purpose of conducting clinical tests on trypanocidal drugs and to arrange for him to be afforded all necessary facilities for his work, including the concentration in some suitable centre of a sufficient number of sleeping sickness cases who could be kept under observation.

It is also recommended that the Secretary of State for Dominion Affairs should ascertain from the Government of Southern Rhodesia whether it would be possible for the Trypanosomiasis Bureau to test the veterinary effects of some new drugs; and from the Government of South Africa whether these tests could also be undertaken at the Veterinary Research Institute, Onderstepoort.

ii. *Protozoological research.*—It is recommended that in order to enable Dr. DUKE to complete his present experiments, the Human Trypanosomiasis Institute, Entebbe, should be maintained on its present basis till the 31st Dec., 1935, when the Institute as such should be closed; and that thereafter the Medical Department in Uganda should undertake such research as its resources permit.

It is recommended that the fullest support should be given to the work of Dr. CORSON at Tinde, and that the investigations on immunity and the relation of trypanosomes now being carried out by Mr. HORNBY at the Veterinary Laboratory, Mpwapwa, should also form part of the program of research.

The sub-committee also makes recommendations regarding other protozoal research.

The report closes with two Appendixes.—The first reprinting the program of tsetse and trypanosomiasis research in East Africa prepared by the Entebbe Conference; and the second giving an account of diagnostic methods in human trypanosomiasis by Sir Arthur BAGSHAWE. W. Yorke.

SELWYN-CLARKE (P. S.). **Trypanosomiasis in the Gold Coast (with Special Reference to 1933-34).**—*Gold Coast Rep. Med. Dept. for Year 1933-34.* Appendix IX. pp. 100-107. With 1 map.

This article opens with a general account of the history of trypanosomiasis in the Gold Coast. In a table the author shows that the incidence of recorded cases of sleeping sickness per 10,000 of all cases treated has steadily increased from 3.2 in 1924-25 up to 56.1 in 1933-34. He points out, however, that particular attention has been paid to the subject on the Gold Coast during the last few years, and that consequently the marked increase in the number of cases reported cannot be attributed entirely to the occurrence of localized epidemics.

After discussing briefly the distribution of the disease in the Colony, the author passes to a summary of the work done during the year 1933-34. In April, MCKERNAN examined 300 persons in the hyperendemic area of Mamprusi under mandate, and found the infection rate (judged by examination of gland juice only) to be about 11 per cent. In August and September of the same year Dr. PURCELL carried out a rather more detailed survey over a large area. He found little evidence of the disease in the eastern and central parts of Northern Mamprusi. In the northern part of the district the incidence of persons suspected to be suffering from the disease was 1.5 per cent. The disease was found to be scattered somewhat scantily throughout Southern Mamprusi, except in the Mandated Territory, where it appeared to be hyperendemic. Towards the end of 1933, a temporary field hospital was established at the centre of this hyperendemic area. A general description of the measures taken to deal with the situation follows.

W. Y.

DUPUY. La maladie du sommeil dans les régions soumises à l'action du Fonds Reine Elisabeth pour l'assistance médicale aux indigènes du Congo Belge (Foreami). Rapport pour l'année 1933. [**Sleeping Sickness in the Regions dealt with by the Queen Elizabeth Funds for the Medical Assistance of the Natives of Belgian Congo (Foreami). Report for 1933.**—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 39-84.]

This lengthy report describes the results of the anti-trypanosomiasis work done with the aid of the Queen Elizabeth Fund during the year 1933 and compares the position during that period with that during the two previous years.

In his preliminary remarks Dupuy defines the conditions under which lumbar puncture is performed; these are:—

(a) *Lumbar punctures for diagnosis.*—These are punctures made on new cases recognized by gland puncture and on suspected cases in whom gland puncture was negative.

(b) *Lumbar punctures of elimination.*—After treatment consisting of large doses a puncture of 1st elimination is made at the end of the course of treatment. After an ordinary treatment of 12 injections of 2 gm. the 1st puncture of elimination is made 3 months later. If the puncture of 1st elimination revealed changed spinal fluid the patient is put on treatment again, and a puncture of 2nd elimination is performed 3 months after its termination. If this puncture also reveals a changed spinal fluid the patient is considered to be in a chronic condition; a third course of treatment is given and this in turn is followed by a puncture of 3rd elimination.

(c) *Lumbar punctures of control.*—When the puncture of elimination reveals a normal spinal fluid the patient is considered as provisionally cured for a period of 6 months and then is subjected to a puncture of 1st control. If the result of this is favourable he is subjected to two further punctures at intervals of 6 months, and then if the fluid is still normal he is regarded as definitely cured. If the puncture of control gives an unfavourable result the patient is again put on treatment and further punctures of elimination and control performed according to the above scheme.

In order to combat arsenic resistance which has been recorded by various medical officers, it was decided to add germanin to the trypanarsyl usually given and to increase the dose of the arsenical. Two types of treatment were used:—The first is that recommended by VAN HOOFF, viz. : recent cases : 1 gm. of germanin followed 2 or 3 days later by 4.5 gm. of trypanarsyl, and then at weekly intervals two further injections of trypanarsyl with sodium hyposulphite; grave advanced cases : 1 gm. of germanin followed 3 or 4 days later by 4 gm. of trypanarsyl with sodium hyposulphite, then at weekly intervals 2 gm. of trypanarsyl up to a total of 24 gm. The second line of treatment is that advocated by RODHAIN and consists of 2 doses of 1 gm. of germanin on consecutive days followed by a series of injections of trypanarsyl according to the preceding scheme.

In all, 620,549 persons have been examined and 15,285 patients treated, but nothing is to be gained by analysis of these totals as certain places had not been examined previously. The Lower Congo has, however, now been under investigation by Foreami for 2½ years, and consequently it is possible to compare the state of affairs in 1933 with that of previous years. Among the 548,556 persons examined, 1,646 new patients were discovered; this gives a contagious index of 0.30 per cent. as compared with 0.59 per cent. for 1931 and 0.41 per cent. for 1932.

The number of patients remaining on treatment on 31st Dec., 1932, was 6,212 as against 7,288 in 1931; that of patients put again on treatment was 1,262 as against 1,404 in 1932. The total number of patients treated was 9,120 as compared with 12,301 in 1931, and 10,873 in 1932. The endemic index was thus 1.66 per cent. in 1933, as against 2.45 per cent. in 1931 and 2.08 in 1932. The number of provisionally cured patients was 4,934 as against 3,855 in 1932.

Efficacy rate = $\frac{\text{cured} \times 100}{\text{number treated}} = \frac{4934 \times 100}{9120} = 54.1$. In 1932 this figure was only 35.5.

The number of patients who disappeared was 354 in 1933, and 381 in 1932; of those who died 301 as compared with 340. Some 3,531 patients remained on treatment on 31st Dec., 1933, the maintained endemic index thus being 0.64 per cent. as against 1.55 per cent. for 1931 and 1.2 per cent. for 1932.

Having summarized in this way the total results obtained, Dupuy passes to an analysis of the results in the various subsectors. An interesting table is given regarding the efficacy of treatment=

$$\frac{\text{cured under control} \times 100}{\text{number treated.}}$$

This figure had improved considerably in all the subsectors except Mayumbe and Lufimi where treatment was handicapped by the existence of chronic arsenic-resistant cases.

After giving some interesting information regarding the results of lumbar puncture, Dupuy passes to the subject of arsenic resistance. This has now been recognized at various foci, viz., Mayumbe 71 new cases in 1933, Cataractes-Nord 7 new cases, Cataractes-Sud 35 new cases, and Lufimi-Basse-Sele 4 new cases. The total of new arsenic resistant cases discovered during the year was thus 121.

The last portion of this long report is concerned with details regarding the various subsectors and must be consulted in the original by those interested.

W. Y.

JAMOT (E.). Note sur la maladie du sommeil en A. O. F. [S.S. in **French West Africa.**—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 499-507.

In 1920 a Commission, presided over by LAVERAN, published a detailed account of the position of sleeping sickness in the French West African Colonies. At that time the disease was recognized in French Guinea, in the Ivory Coast, and in parts of Senegal. Isolated cases had been found in Dahomey and the disease had also been recognized at certain places in Haut-Sénégal Niger. In 1926 HERIVAUX discovered the great focus in Togo which extended to Dahomey, and in 1931 SOREL and ROBINEAU drew attention to the fact that the disease was endemo-epidemic in Haute-Volta, in Dahomey, and on the Niger.

In this paper Jamot summarizes the situation as it exists in the various French West African Colonies at the present time. After dealing with each of the Colonies separately he states that the total number of cases recognized on 31st Dec., 1934, was more than 50,000. They are distributed as follows:—Niger 369, Soudan 2,580, Guinea 4,002, Dahomey 6,331 and Ivory Coast 38,167. If to these are added the 16,000 patients found in Togo in May, 1934, the total figure for French West Africa is no less than 68,000 [? 66,000]. When it is remembered that only part of the infected regions have been visited, that in the Ivory Coast which has been most investigated not more than two-thirds of the people have been examined, and that the limitations of the method of examination must allow many cases to escape recognition, it is obvious that the true figure is much greater than 68,000.

W. Y.

BEVAN (LI. E. W.). **Notes on the Human Trypanosomiasis of Southern Rhodesia.**—*Jl. Comp. Path. & Therap.* 1935. June. Vol. 48. No. 2. pp. 97–111. [20 refs.]

After giving a general account of the development of knowledge of sleeping sickness due to *T. rhodesiense* since its discovery in November, 1909, the author passes to a consideration of human trypanosomiasis in Southern Rhodesia. Since 1912, there have apparently been only 7 European cases, all of whom contracted the disease in the Sebungwe and West Hartley districts. No cases have been recorded from the Lomagondi and Darwin districts in parts of which *G. morsitans* are plentiful, and where the author has found domestic animals to become infected with the *brucei* type of trypanosome. During the same period 49 native cases have been recorded.

During the last two years some alarm has been caused by the death from trypanosomiasis of a European, Mr. L —, who is believed to have contracted the infection at Gowe. Another European, Mr. A—, also developed the disease in this neighbourhood. During 1933 a number of cases of sleeping sickness were met with amongst native hunters in the Gowe district. Having thus located Gowe as the focus of recent infection, it is interesting to note that, according to the Chief Entomologist, there are certain small areas depicted in his maps where the tsetse fly survived after the rinderpest in 1896; and the Gowe area is one of these. Another such area is the Manzituba Vlei and environs in the Sebungwe district, and it is in this vicinity that the medical expedition of 1913 found its cases.

Bevan believes that it is in these places that the local natives would be liable to infection from birth and any premunity would be maintained by constant re-infection. It is in such places that one would expect to find carriers, and as a matter of fact carriers were actually found in these districts by the Commission of 1913 and by Dr. BLAIR in 1934. Other parts of the country appear to be free from human trypanosomiasis, and it is probable that with the clearing up of these comparatively limited areas this undesirable menace will soon be entirely eliminated from Southern Rhodesia. W. Y.

LESTER (H. M. O.). **Report of the Tsetse Investigation.**—*Nigeria Rep. Med. & Health Services for Year 1933.* Appendix B. pp. 74–83.

Topics discussed here are:—Tartar emetic treatment of cattle; histopathology of bovine trypanosomiasis; relation of *T. gambiense* and *T. rhodesiense*; tsetse surveys; testing of new drugs; infection rates in man in Nigeria and measures to cope with the spread of infection.

During the year there have been further big increases in the amount of sleeping sickness work done in the field in Nigeria, and as far as possible research has been continued in the Gadau laboratories, although only a skeleton research staff is at work there. In May, Dr. NASH, Entomologist, joined the investigation.

Further experiments have been conducted on the treatment by tartar emetic of cattle infected with *T. congolense* and *T. vivax*. The results are disappointing. At the request of the Chief Veterinary Officer a small experiment was carried out to test the possibility of transmitting bovine trypanosomiasis directly from one animal to

another by means of an unwashed hypodermic needle. A "record" needle was inserted into the muscles of an ox, the blood of which contained numerous *T. vivax*. It was then removed and inserted immediately subcutaneously into a clean animal and subsequently into a second clean animal; both became infected.

Dr. MERRETT has continued work on the histopathology of bovine trypanosomiasis (*T. vivax* and *T. congolense*). The post-mortem findings were extremely variable, but sufficient constant features were present to warrant a division into (a) completely negative autopsy, (b) slight involvement of the heart, and (c) marked cardiac lesions, associated with variable changes in other organs. Tissues from all the organs were sectioned and examined microscopically. Changes in the brain were not seen. The heart was the organ chiefly affected, showing all changes of myocarditis up to a condition of fibrosis and muscular fragmentation.

Work on the characteristics of Nigerian strains of the polymorphic trypanosomes has been continued. In all, 17 such strains have been investigated, and it has been found that certain strains exhibited characteristics intermediate between *T. rhodesiense* and *T. gambiense*. As a result of this work it is believed that *T. rhodesiense* is only a virulent type of *T. gambiense*. A full report has already been published [this *Bulletin*, Vol. 31, p. 198].

An attempt is being made to maintain various strains of trypanosomes by constant cyclical transmission through *G. tachinoides* and *G. morsitans*. The characters which are being investigated are virulence to small laboratory animals and reaction to trypanamide.

The Entomologist has carried out tsetse surveys, and as the result of a prolonged tour through the south-eastern and southern districts of Kano Emirate recommendations have been made for a number of local clearings intended to reduce fly-man contact to a minimum. It is believed that judicious clearing of narrow belts of riverine vegetation would reduce the incidence of sleeping sickness in these areas to very small proportions; frequently, the existence of *G. tachinoides* depended upon a belt of quite light vegetation, which in many cases was only 10 yards in width. Research is being carried on with the object of studying the relationship between tsetse and different types of vegetation, and to ascertain the reasons for the tsetse preferences by measuring the climatic conditions in favourable and less favourable vegetation types.

The testing of new chemical compounds.—A system of co-operation with certain large chemical firms in Europe has been inaugurated, and arrangements have been made for promising new drugs to be sent to Gadau to be tested against freshly isolated strains. If the results seem encouraging, the drugs will then be tested against human and animal trypanosomiasis in the field.

Observations have been made on two new chemical compounds supplied by Messrs. Bayer-Meister Lucius. The first of these, Surfen C, a quinoline derivative, was found to be very active in laboratory animals infected with trypanosome strains isolated from man; but in man himself the strains did not appear to be nearly so sensitive, and the use of the drug in human trypanosomiasis is contra-indicated, as it is liable to produce acute nephritis. The drug is being tested against *T. vivax* and *T. congolense*, and it seems possible that it may prove to be a valuable remedy in animal trypanosomiasis.

Experiments have been started with the second drug Std. 386B, an organic compound of arsenic and antimony. The results are, as yet, incomplete.

The next portion of the report summarizes the work on sleeping sickness. During the year, 27,919 cases of sleeping sickness have been treated. To begin with there were three sleeping sickness teams in the field, but by the end of 1933 five complete teams, each consisting of one medical officer, two nurses and 24 dispensing attendants, were at work, whilst a 6th team was due to start in January, 1934. Part of this service has been paid for by the Native Administrations.

The infection rates which have been found give some indication of the magnitude of the problem with which they have to deal. In various districts this ranges from 16 to 29 per cent. There is a good deal of indirect evidence to show that the disease has spread rapidly during the last few years. In many areas the death rate has been high and there has been a definite decrease in the population, especially in the Zaria Emirate, where shrinkage in the population has been alarming.

An attempt is being made to cope with the disease by mass treatment and by localized protective measures against the tsetse fly. Experience has shown that mass treatment itself is quite effective in reducing the incidence of the disease. ELLIS, working in Hadeija, found that of 829 positive cases which had been given a course of 23 gm. of trypanamide, only 15, *i.e.*, 1.8 per cent., had trypanosomes in their gland juice or blood at the end of treatment. In other parts of the country, however, many more cases had been found to be resistant to treatment with trypanamide. For this reason arrangements had been made to use a combined treatment of antypol and trypanamide on a large scale.

The article closes with a detailed report of Dr. PAISLEY, the Senior Sleeping Sickness Officer. W. Y.

DUMONT (Robert). Influence des conditions alimentaires sur la gravité et l'extension de la maladie du sommeil. [**The Influence of the Food Supply on the Gravity and Extension of Sleeping Sickness.**]*—Rev. Méd. et Hyg. Trop.* 1935. Jan.-Feb. Vol. 27. No. 1. pp. 36-37.

In this note the author stresses the importance of nutrition in a combat against sleeping sickness. He quotes from HUOT (1924) the effect that insufficient crops with malnutrition is a condition constantly found in all places gravely infested by sleeping sickness, and furthermore that it appears that trypanosomiasis does not kill in populations normally nourished.

MARTIN concluded that under-feeding of the natives greatly increased the evil effects of trypanosomiasis. JAMOT cites a striking example. In the valley of the Koumi, 9 villages at the beginning of 1913 contained 5,933 inhabitants. Towards the middle of the year, the first cases of sleeping sickness were imported. In 1924, Poux records that the population was industrious and prolific and covered the country with magnificent plantations. In this region sleeping sickness had not done much harm. There are two factors which play a part in the epidemiology of the disease—the parasite and the resistance of the subject. Other examples are given.

Dumont concludes that in the combat against sleeping sickness one should not rely entirely on medicaments, no matter how active

they may be, but also on the resistance of the organism conferred by good feeding. W. Y.

DUKE (H. Lyndhurst). *On Trypanosoma brucei, T. rhodesiense and T. gambiense and their Ability to Infect Man.*—*Parasitology*. 1935. Feb. Vol. 27. No. 1. pp. 46–67. [30 refs.]

In this work the author has continued his inquiry into the relationships of the African polymorphic trypanosomes to one another and to man. He has worked with 11 strains and has examined the transmissibility of each by *G. palpalis*, and also the power of each to infect man, after it had been maintained in the laboratory for various periods and by different methods. The results of his observations are summarized as follows:—

"1. A strain of *T. rhodesiense* [Tinde III], isolated from man and readily transmissible by tsetse, was passed by direct inoculation through a series of fourteen guineapigs over a period of 18 months. At the end of that time it had lost its transmissibility by *Glossina palpalis*, and it also failed to infect a volunteer.

"2. Another line of the same strain, after 98 days in a bushbuck, 30 days in a fowl and 294 days in oxen, proved still readily transmissible by *G. palpalis* and also readily infective to man.

"3. A second strain [Tinde I] underwent seven consecutive cyclical passages through tsetse, then two passages by the syringe, and finally another cyclical passage, all save one in monkeys. When tested on man at the tenth and eleventh passages it was found to be non-infective.

"4. A strain of *T. gambiense* [Braun], isolated in November 1920 from a patient from Fernando Po, was found in February 1934 to be readily infective to man. The strain was entirely non-transmissible by and almost completely non-infective to *G. palpalis*.

"5. Three strains of *T. brucei* [LV, LVI, LVII], one from the west, one from the north and one from the south of Uganda Protectorate, were found to be incapable of infecting normal healthy man. All the tests were carried out with cyclically infected tsetse.

"6. A freshly isolated strain of *T. gambiense* [LII] from a Uganda native was transmitted to man by cyclically infected laboratory-bred *G. palpalis*.

"7. A strain of *T. rhodesiense* [LX], shortly after its recovery from a native of Tanganyika Territory, underwent three successive cyclical passages by laboratory-bred *G. palpalis* from monkey to monkey; at each passage the strain was tested on man and found to be readily infective.

"8. A strain from Nigeria [BR] showing points of resemblance to both *T. gambiense* and *T. rhodesiense* was found to be pathogenic to man, on subcutaneous inoculation of infected blood, three years after its first isolation."

Duke lays stress on the fact that this work constitutes the first record of the experimental infection of man either with *T. gambiense* or with *T. rhodesiense* by the bite of a cyclically infected tsetse. It also contains an account of the loss by two accredited strains of *T. rhodesiense* of the power of infecting man. The fact that *T. rhodesiense*, under conditions which may reasonably be described as natural, may lose its power of infecting man is of considerable interest. The possibility was to some extent fore-shadowed by the work of the reviewer and his colleagues [this *Bulletin*, Vol. 27, p. 804], but the only reliable criterion in the matter is the test on the human subject applied as nearly as possible in the way nature applies it.

The loss of pathogenicity to man by strain Tinde III is the first substantiated record of this phenomenon. Duke states that this is

apparently ascribable to the effect of passage through guineapigs, for under different conditions the strain retained this property. Reference is made to the fact that CORSON has found that a strain of *T. rhodesiense* was still pathogenic to man after maintenance in goats by direct inoculation for a period of 19 months; and also to the fact that CORSON in a later paper refers to the increased susceptibility to human serum caused by guineapigs. There is thus some evidence that maintenance of a trypanosome in guineapigs has an unfavourable effect on certain of its activities, viz., reducing its transmissibility by *Glossina* and probably impairing its ability to infect man.

Although after passage through the guineapigs the infectivity of strain Tinde III to *G. palpalis* was diminished enormously, passage through oxen produced no such effect. This is especially interesting in light of Duke's previous experience of the effect on man's trypanosomes of sojourn in calves: in these experiments the indices of a strain examined in the blood of a calf were invariably reduced [this *Bulletin*, Vol. 31, p. 566].

The striking contrast between the behaviour of the *T. gambiense* strain (Braun) and that of Tinde III in guineapigs is a matter of interest. Prolonged residence in small laboratory animals, extending over 14 years, had failed to impair the pathogenicity of the former strain for man, although the strain had completely lost its transmissibility by *G. palpalis*. The observations indicate the relative antiquity of *T. gambiense* as a parasite of man and the comparative instability of the power of *T. rhodesiense* to infect man, and show how easily this trypanosome may revert to a form indistinguishable from typical "wild" *T. brucei*. These facts tell against KLEINE's hypothesis that *T. gambiense* and *T. rhodesiense* are one and the same species, zoologically distinct from *T. brucei*. Duke finds in the present observations support for the view advanced by him in 1921, viz., "*T. gambiense*, *T. rhodesiense* and *T. nigeriense* are to be regarded as particular strains of *T. brucei* which have become, after sojourn in other hosts, more or less adapted to life in the blood of man."

No one has yet witnessed the exhibition by an unequivocal *T. brucei* of the power to infect man, but the issue is confused by the convention whereby any *T. brucei*-like trypanosome recovered from game or wild tsetse, and proved capable of infecting man, is at once styled *T. rhodesiense* and assumed to have had previous acquaintance with man. Duke states that he has long believed that there are in nature strains of *T. brucei* which, given the opportunity, can use man as a host, and it is now quite certain that a trypanosome can and does change in relation to a particular host, i.e., man. TAUTE's big experiment in which 129 natives, including weaklings and diseased, withstood exposure to 6 strains of *T. brucei* seems to Duke to justify the conclusion that if man is to become infected by *T. brucei* the onus is on the trypanosome to overcome some degrees at least of the range of resistance possessed by a normal human community.

Duke believes that the resistance of man to *T. brucei*, though considerable, is not absolute, and in *palpalis* regions man has paid the penalty of this imperfection by becoming the principal mammalian host for the representative of *T. brucei* in those regions, *T. gambiense*. The paper concludes as follows:—

"As matters stand at present, the claim of *T. rhodesiense* to distinction as a species, or even a subspecies, is indeed feeble. The name is, however, useful until it is decided whether *T. brucei* or *T. gambiense* can best absorb

it zoologically. The evidence recently acquired at Entebbe seems to me to identify this trypanosome with *T. brucei*. If this be the correct interpretation, then the two types of human trypanosomiasis are to be ascribed to *T. gambiense* and to *T. brucei* respectively. For the former trypanosome, by virtue of its long establishment as a parasite essentially dependent on man in primitive African conditions, surely possesses a fair claim at all events to 'dominion status' if not to complete severance from its parent stock." W. Y.

DUKE (H. Lyndhurst). **Further Studies of the Behaviour of *T. rhodesiense*, recently isolated from Man, in Antelope and Other African Game Animals.**—*Parasitology*. 1935. Feb. Vol. 27. No. 1. pp. 68-92. [20 refs.]

The work dealt with in this paper is a continuation of similar work published in 1933 [this *Bulletin*, Vol. 30, p. 769]. Its object is to determine the effect on the trypanosomes of man of prolonged residence in antelope. Duke has had two main questions in mind; firstly, whether prolonged residence in antelope interferes with the power of the trypanosome to infect cyclically *Glossina*; and secondly, whether it interferes with the capacity of the trypanosome to infect man.

After briefly reviewing previous work bearing on these important problems, Duke passes to a detailed account of his own work. The following summary is given:—

"1. Evidence is produced to show that *T. rhodesiense* may retain its cyclical transmissibility by *Glossina* for at least 600 days in an antelope.

"2. Prolonged residence in these animals tends to impair the power of a strain to infect man, when infection is attempted by the cyclical route. Thus of six volunteers exposed to cyclically infected tsetse carrying *T. rhodesiense* that had been for many months continuously in antelope, only one became infected. *All these flies derived their infections from the antelope itself.* As the cyclical method is the one operating in nature, these observations suggest that although certain species of antelope are admirable hosts for *T. rhodesiense*, yet as a reservoir from which tsetse can become infected with trypanosomes pathogenic to man these animals do not constitute so great a menace as has hitherto been supposed.

"3. In contrast to (2), in every instance where the trypanosomes from the antelope, before being tested on man, were inoculated by the syringe into a monkey, every volunteer exposed became infected.

"In the single experiment where the monkey was infected by tsetse instead of by direct inoculation from the antelope, one volunteer became infected and another did not. There is thus a suggestion that the passage through the monkey prepared the trypanosome for survival in man. On the other hand, the behaviour of strain Tinde I shows that *T. rhodesiense* may lose its power to infect man in spite of repeated passage through monkeys.

"4. Some further indirect evidence is produced to show that *T. rhodesiense* may owe its origin to *T. brucei*, and that pathogenicity to man may be a property possessed in different degrees by different strains of *T. brucei* in nature.

"5. These researches suggest, also, that human beings differ in their susceptibility to *T. rhodesiense*, but that these differences only operate within a narrow range of variation in the power of strains to infect man. In other words, strains strongly pathogenic to man will infect anyone,

but strains whose power has been weakened will only be able to use individuals of subnormal resistance.

" 6. Two different strains of *T. rhodesiense* have been shown to behave differently in the same man. One did and the other did not infect him.

" 7. There may be a difference in the suitability of the various species of antelope to act as hosts to *T. rhodesiense*. Thus the bushbuck seems to be a better host to the trypanosome than the oribi.

" 8. A young hyaena infected with *T. rhodesiense* for 180 days remained in excellent health. Flies infected from a monkey sub-inoculated with the blood of this hyaena infected a volunteer: the trypanosome had then been 80 days in the hyaena.

" 9. Clean flies that had taken their first two meals off monkeys infected with a strain of *T. rhodesiense* non-pathogenic to man, were nourished entirely on human blood during the first 3 weeks of the cycle of development of the trypanosomes in their interior. These flies, on the completion of this cycle, were still unable to infect man.

" 10. A strain of *T. rhodesiense*, after a series of cyclical passages through a reedbuck and six monkeys, was found to be non-pathogenic to man. The possibility has to be borne in mind that this strain owed its original association with man to meeting an abnormally susceptible individual. This strain since its arrival at the Institute has been tested on nine different volunteers, and none of them became infected. There is therefore nothing to distinguish it from *T. brucei*, save the fact of its isolation from man.

" 11. It is recorded that a single cyclically infected fly infected a volunteer at a single feed.

" 12. It is shown that the appearance of a tender indurated swelling at the site of the bite of an infective fly is a not uncommon symptom of an infection with *T. rhodesiense*. Local tenderness and swelling were also noted where the glands of an infected fly had been inoculated subcutaneously, even in cases where no infection ensued. Where inoculations of blood were employed on man the local disturbance disappeared rapidly when no infection resulted, but when infection took place the local symptoms steadily increased during the last few days of the incubation period, and before trypanosomes were recognized in the peripheral blood.

" 13. The only infection of an antelope with *T. gambiense* carried out during this research was that of oribi III with strain LI. This strain at its first isolation was not very transmissible by *G. palpalis*, and after a few months in the antelope showed signs of failure to adjust itself of this particular host. Another strain, mentioned in a previous paper (Duke, 1935), failed to infect an adult female situtunga, although two sheep exposed to the same strain at the same time duly became infected."

W. Y.

DUKE (H. Lyndhurst). **Studies on the Factors that may Influence the Transmission of the Polymorphic Trypanosomes by Tsetse.**
IX.—On the Infectivity to *Glossina* of the Trypanosome in the Blood of the Mammal.—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 131–143.

In this paper Duke gives a selection of the various transmission experiments carried out at Entebbe which, in his opinion, illustrate what appear to be different phases of the phenomenon of transmissibility. ROBERTSON (1912) wrote "Given reasonably favourable conditions of temperature and moisture, it is the strain of trypanosomes and not the fly that within a relatively wide range plays the deciding

rôle in limiting the number of infected glossina." Duke states that in his earlier work he adopted as a working hypothesis the assumption that there are certain forms of the trypanosome in the mammal especially fitted to infect tsetse, and that when a fly takes up a sufficient number of these forms it becomes infected. More recent experience showed, however, that the problem is by no means so simple. The part played by the fly is undoubtedly of considerable importance, and TAYLOR (1932) has produced evidence that temperature also exerts an influence.

During 15 years of experimental work, Duke has acquired certain impressions regarding the laws which govern the transmission of trypanosomes by tsetse. He considers that he has demonstrated that there exist in nature in Africa strains of trypanosomes which, at the time of their original isolation from the vertebrate, man or antelope, are non-transmissible by *G. palpalis*. Such strains remain consistently non-transmissible. The disappearance of transmissibility has actually been witnessed in a number of strains of *T. gambiense* during their maintenance in the laboratory. These observations all point to an inherent and permanent change in the trypanosome itself, quite unconnected with the variability of the insect vector.

Four series of transmission experiments are discussed in the present paper. Series I consist of paired experiments. Two batches of flies were fed at the same time on the same infected animal; thereafter one of the batches was nourished on a clean animal, while the other was fed again on one or more occasions on an infected animal. In Series II each of the tests consisted of 4 or 5 experiments instead of a pair as in Series I. The flies of one experiment of each test fed on 3 or 4 different days on the infected animal, and on each of these days a box of clean flies fed on the same animal only once. The general conclusion from these two series of experiments is that they furnish no evidence that multiple feeding results in a higher infection rate than does single feeding.

The experiments of Series III represent another attempt to raise the infection rate of *G. palpalis* by repeated exposure to the chance of infection. The results confirm the conclusion reached from the first two series of experiments.

The experiments grouped into Series IV were selected from the records of the Entebbe Institute to illustrate various phenomena of common occurrence. They are summarized in a table which is divided into four sections. Section A illustrates consistent infectivity of the trypanosome to tsetse; Section B illustrates periods of intensified activity; Section C illustrates non-infective periods, and Section D illustrates the results of feeding flies on man for several consecutive days; a fresh box of flies being fed each day.

The author's conclusions are as follows:—

"1. A study of the Entebbe records of transmission experiments with man's trypanosomes and *G. palpalis* lends support to Robertson's views on the endogenous cycle expressed in 1912.

"Of special interest is the evidence of the existence of 'negative phases' in the development of the trypanosome in the mammal, phases during which the trypanosomes though often numerous in the blood are non-infective to the tsetse.

"2. An examination of the experimental section of this paper suggests that repeated feeds on an infected animal during a positive phase of the cycle do not increase the infection rate of the flies over that produced by one such feed."

W. Y.

- i. BORREMANS (P.) & VAN BOGAERT (L.). Les manifestations extra-pyramidales de la trypanosomiasis chez l'Européen. (Syndrome d'inhibition avec stéréotypies, pigmentations cutanées symétriques et anneau cornéen.) [*Cases of Extra-pyramidal Syndrome and Psychosis in S.S.*]—*Jl. Belge Neurol. et Psych.* 1933. Vol. 33. No. 8. pp. 561-588. With 12 figs. [38 refs.]
- ii. BAONVILLE (H.), LEY (J.) & TITECA (J.). Psychose hallucinatoire chez un trypanosomié.—*Ibid.* 1934. Feb. Vol. 34. No. 2. pp. 129-138.

i. A detailed clinical account is given of a patient who exhibited a particularly well marked extra-pyramidal syndrome. The case is assumed to be one of trypanosomiasis, but the diagnosis appears to be based on the clinical history and the pathological findings at the autopsy; there is no evidence that a definite diagnosis was ever made.

The patient had spent 12 years in Uganda and Urundi. During 1927, he had two severe febrile attacks and pronounced erythema of the abdomen and lower extremities. These attacks were accompanied by severe headache, but there is no record of any adenitis; lumbar puncture was not performed. In 1929 the patient became very irritable; he manifested violent paroxysms of anger, especially when in an alcoholic condition; he slept badly and became very emaciated. During his last year in Africa he indulged in sexual excesses of all sorts and in sadism, and had a severe attack of dysentery. A course of neosalvarsan was given without benefit and he was invalided home. Shortly after his arrival in Belgium, things became worse. He exhibited visual hallucinations and later mental confusion and somnolence. Sphincter trouble finally developed and the patient owing to his obscurities and violence had to be put in a mental home. Lumbar puncture gave a negative Wassermann, protein: 1.04 gm., Pandy: + + +, lymphocytosis: 113. As he became a little better he was discharged, but had to be re-admitted two months later. Blood examinations were negative and arsenical treatment was of no avail.

During his second sojourn in hospital, the patient exhibited several epileptiform attacks. He lay on his back with his limbs completely extended for hours without making any movement. When spoken to, he replied correctly in a monotonous voice; there was a complete absence of spontaneity, and he made only those movements which were absolutely necessary. There were no tremors but a permanent hypertonic state of the muscles. Examination of the eyes was interesting; the cornea was surrounded by a greenish-brown pigmented circle, but the movement of the eyes was completely normal and the pupils reacted normally. All the cranial nerves were intact; the reflexes were normal as was also sensation. He was habitually in a torpid mental state, and it was only during the acute periods that there was a tendency towards paranoia. There was very deep brown pigmentation of the skin of the legs and feet, which stopped at the level of the prominence of the tibia; the penis was similarly pigmented.

The condition remained more or less like this for 3 months when there was a sudden febrile disturbance with dyspnoea and death.

There follows a lengthy account of the post-mortem findings; these consisted of a meningo-encephalitis with pronounced meningeal infiltration, and an intense infiltration of the central grey nuclei.

The findings in this case are compared in detail with those of other observers and the conclusion is reached that the case was one of trypanosomiasis.

ii. A description is given of a case which exhibited a paranoid syndrome and which, from the history and development of the disease, was believed to be one of trypanosomiasis.

It is noted that the patient—a native of the Belgian Congo—left Africa in 1922 and remained in Europe in a state of apparent good health for 10 years. Delusions of persecution then developed insidiously. A lengthy clinical account of the case is given and this is followed by a discussion regarding the correct diagnosis. [These papers must be consulted in the original by those interested.] W. Y.

RASKIN (A.). **The Clinical Aspect of Trypanosomiasis.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1-2. [In Russian pp. 117-120. English summary p. 120.]

A detailed description of the clinical course and treatment of a case of human trypanosomiasis contracted by an accidental laboratory infection with a mouse-strain of *T. gambiense*. The incubation period in this case was 8 days. The patient was successfully treated with "Bayer 205" combined with neosalvarsan. C. A. Hoare.

VAN SLYPE (W.). *Instabilité liquidienne de certains trypanosés traités par la tryparsamide.* [Instability of the Cerebrospinal Fluid in Cases of Trypanosomiasis treated with Tryparsamide].—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 432-434.

In the course of treating 378 sleeping sickness patients with tryparsamide, the author encountered five in whom the changes in the spinal fluid were peculiar. Details of the treatment and of the cell contents of the spinal fluid found at 3 subsequent lumbar punctures are given. In 4 of the 5 cases the lumbar puncture made immediately after treatment showed an excess of cells, whereas the punctures made 1 to 3 months later revealed in every case a normal cell count. The third puncture made 3 to 5 months after the second showed in all cases but one an excess of cells.

The author inquires whether these changes can be explained on the following hypothesis:—The excess of cells found at the first puncture is due to a meningeal reaction caused by the drug; this disappears after a month or two and hence the second puncture is normal, whilst the abnormal findings at the third puncture are the result of a nervous relapse due to the infection. On such a hypothesis it is curious that those cases which exhibit a meningeal reaction to the drug should likewise relapse. Are we concerned here with individuals possessed of a peculiarly fragile nervous system, especially sensitive to tryparsamide and at the same time especially liable to relapse? It is unlikely that all these successive changes are due to tryparsamide alone, because a second course of tryparsamide made the spinal fluid normal.

The conclusion reached is that a certain small number of cases of sleeping sickness exhibit an unstable spinal fluid after treatment with tryparsamide, and that consequently several punctures at intervals of several months should be performed after treatment as a second course may prove to be necessary. Details are given of 5 other cases in which so far only 2 post-treatment punctures have been made, but which the evidence so far collected suggests fall into the same category as the above cases. The author therefore believes that 9 of his 378 cases exhibit what he designates as instability of the spinal fluid, i.e., a 'normal post-treatment puncture sandwiched between two abnormal punctures.

W. Y.

SCHWETZ (J.). Sur un nouveau cas de trypanosomiase (humaine) arsénico-résistante. [New Arsenic Resistant Case of Sleeping Sickness.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 123-125.

Information is given regarding a case of trypanosomiasis which was resistant to tryparsamide, but susceptible to foudin.

The patient, who came from the region of Stanleyville, was diagnosed as suffering from trypanosomiasis on the 3rd December, 1932. From the 4th to the 24th December he was given 7 gm. of tryponarsyl. On the 2nd January, 1933, a lumbar puncture revealed 3·4 lymphocytes per cmm. When examined at the laboratory at Stanleyville on the 9th February, 1933, no puncturable glands were found, but fresh preparations of his blood showed numerous trypanosomes. Between the 7th March and the 3rd July, 1933, the patient was given 36 gm. of tryparsamide. On the 5th July there were no puncturable glands, but two trypanosomes were found in 10 cc. of blood examined by the triple centrifugation method. The patient was then put on a course of foudin, and between the 17th July and the 10th August, 1933, he received 10 injections. Examinations made on the 21st August and the 23rd September were completely negative. W. Y.

DE MARQUEISSAC (Henri). Emploi des principaux médicaments spécifiques dans le traitement de la maladie du sommeil et utilisation de ces médicaments dans les traitements associés. [The Use of the Chief Specific Drugs in the Treatment of Sleeping Sickness and the Employment of these Drugs in Combination.]—*Gaz. hebd. Sci. Méd. de Bordeaux.* 1935. Jan. 27 & Feb. 3. Vol. 56. Nos. 4 & 5. pp. 56-60; 67-71.

These papers give an account of the various drugs used in the different forms and stages of human trypanosomiasis and discuss the various indications for the employment of the particular drugs, and the various signs of intoxication which they may produce. The articles are of general interest to the practitioner but contain nothing new, and do not require special mention in this *Bulletin*. W. Y.

VAN DEN BRANDEN (F.) & APPELMANS (M.). Au sujet du tryponurile. [On Tryponurile.]—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 107-112. [12 refs.]

Tryponurile (Meurice) is a product prepared by l'Union Chimique containing equal parts of tryponarsyl and hexamethylene tetramine. It may produce kidney lesions.

The authors gave 5 rabbits an injection of 2 gm. of this preparation. The animals were kept under observation for 15 days and all remained alive. The urine was collected and examined, and in that of 2 rabbits albumen was found. The rabbits were then killed and the kidneys examined. Pronounced degeneration of the epithelium of the uriferous tubules was discovered in all 5 animals. In 2 other rabbits, which had been given an injection of 1 gm. of tryponarsyl only, similar lesions were found, but they were not so pronounced and were more discrete.

A summary of the literature relating to the administration of tryponurile to man is given. The general conclusion reached is that in view of the accidents which had been observed in man, and of the

renal lesions which were found in rabbits, trypanuril must be given with caution in the treatment of human trypanosomiasis. Van den Branden is of opinion that the initial dose of trypanuril for man should not exceed 4 gm. W. Y.

SILBERSCHMIDT (W.). Ueber Chemotherapie durch Inhalation. Versuche mit Trypanosomen. [**Chemotherapy of Trypanosome Infections through Inhalation.**—*Schweiz. Med. Woch.* 1935. June 15. Vol. 65. No. 24. pp. 551-553.]

The object of the experiments described in this paper was to ascertain whether inhalation-therapy was of any use in infectious diseases. The author selected as his experimental infection *T. evansi* in rats and mice, and tartar emetic as the drug to be examined.

The tartar emetic solution was sprayed by means of a water-pump into a 25 litre triangular box, the apex of which was covered with glass. The experimental animal was placed in an open cage at the bottom of the box. The strength of the tartar emetic solution varied from 1 to 5 per cent. and 3 cc. were sprayed into the box within an hour. How much was inhaled by the animal and how much was deposited on the sides of the container, it is impossible to say. The animals were exposed to the spray for 2 to 6 hours once or twice daily for several weeks; some died of dysentery (antimony poisoning), but others tolerated the treatment for 4 weeks.

The results of the experiments, which are summarized in tables, show that the treatment controlled the infection and prolonged the life of the rats and mice very considerably (3-9 days for the controls, over 30 days for the treated animals); *therapia sterilisans magna* was, however, not obtained. W. Y.

LAUNOY (L.) & PRIEUR (M.). Contribution à l'étude de l'essai biologique de la tryparsamide. [**The Biological Testing of Tryparsamide.**—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 389-398.]

Although tryparsamide is perfectly crystallizable and it exhibits constant physical and chemical properties, it is subjected to a biological control, which is essentially a test of its toxicity. This consists in the intravenous injection of 5 well-nourished adult male rabbits with a dose of 0.75 gm. per kilo. of tryparsamide in a 10 per cent. solution; 3 of the 5 animals should survive without signs of serious intoxication. A period of observation is not stated, but is ordinarily 7 days. This control has been accepted by all firms possessing a licence from the Rockefeller Institute.

Reference is made to the work of POTTIER & VAN DEN BRANDEN [this *Bulletin*, Vol. 30, p. 786] who, working with the different brands of tryparsamide, found that rabbits easily tolerated a dose of 1.25 gm. per kilo., and that 100 per cent. of fatalities was obtained only when the dose was 2.5 gm. These authors accordingly suggested that for the efficient test the dose should be 1 gm. or 1.25 gm. instead of 0.75 gm. as hitherto.

During the period September, 1933, to March, 1935, the authors have had occasion to make numerous tests on the toxicity of tryparsamide. Most of their work has been done with the French product. They point out that before the biological investigations are undertaken,

a chemical analysis of the drug is essential. The drug should contain 24.6 to 25 per cent. arsenic; it ought not to lose more than 0.5 to 0.6 per cent. of water after heating for 4 hours in the air at a temperature of 98°C. Anilarsinic acid should be present only in imponderable amounts.

The results of the authors' experiments on the toxicity of tryparsamide for a rabbit are summarized in tables. In all, 162 rabbits were given a dose of 0.75 gm. per kilo. and of these 75 per cent. survived 7 days, 70 per cent. 10 days, 59 per cent. 20 days, and 55 per cent. 30 days. The results obtained for the 308 rabbits which received 1 gm. per kilo were 57 per cent. alive after 7 days, 49 per cent. after 10 days, 41 per cent. after 20 days, and 39 per cent. after 30 days. It is pointed out that the differences obtained after 20 and 30 days of observation are very slight, but the differences between 7 and 10 days and 20 and 30 days are considerable. The conclusion is that the observation period should be 20 days, the usual 7 days being insufficient. The dose of 0.75 gm. gives more regular results than does the larger dose. It is probably therefore to be preferred.

The authors give an account of the technique used by them in the preparation of their solution of tryparsamide. In this they point out what is generally well known, viz.: that if one wishes to make a 10 per cent. solution of tryparsamide, he should not add 10 gm. of the drug to 100 cc. of water (the final volume of such a solution would be 107.75 cc.)

Information is next given regarding the toxicity of tryparsamide for mice. The results of an enormous number of experiments with the French product manufactured between 1933 and March, 1935, are summarized in the following table:—

Number of mice treated	Doses in cgm. per 20 gm. mouse	Percentage of survivals after 10 days	Percentage of survivals after 30 days
105	6	80	71
895	7	64	54
495	8	60	49
155	9	50	43
145	10	38	33

The paper ends with some observations on the trypanocidal action of tryparsamide on *T. brucei* infections in mice. W. Y.

LOURIE (E. M.), MURGATROYD (Frederick) & YORKE (Warrington). **Studies in Chemotherapy. XII.—The Diffusibility of the Aromatic Arsenicals into Erythrocytes and the Action of the Latter on the Pentavalent Arsenicals.**—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 265-282. [10 refs.]

These experiments show that the aromatic arsenicals, reduced tryparsamide and tryparsamide, diffuse into the red cells, that that part of the tryparsamide which enters the red cells is changed into a more actively trypanocidal substance, that a solution of red cells is capable of greatly increasing the trypanocidal power of tryparsamide, possibly by converting it into reduced tryparsamide, and that haemoglobin is not responsible for the change, which depends on a constituent that is relatively thermostable.

In the previous article of this series [*ante*, p. 26] the trypanocidal titre of the serum of rabbits was recorded after the intravenous injection of certain aromatic compounds of arsenic. It was found :—

" 1. That the effect of injection of an arsenobenzol compound (N.A.B.) or of an aromatic trivalent arsenical compound (reduced tryparsamide thioglycollate) is to confer immediately upon the serum an enormously high trypanocidal titre ; this titre, which is proportional to the dose given, immediately falls—quickly at first and more slowly later—until it ultimately returns to zero. The fall in the case of reduced tryparsamide thioglycollate is much more rapid than in that of novarsenobillon.

" 2. That the immediate effect of injection of an aromatic pentavalent arsenical compound (tryparsamide) is to confer but a relatively low trypanocidal titre upon the serum ; instead of falling, however, as happens with the other two drugs, the titre steadily rises and does not attain to its maximum for some time after injection. The titre reached is, moreover, in no way comparable with the enormous titres obtained with novarsenobillon and reduced tryparsamide thioglycollate. [These observations are illustrated by the graph on page 27, above.]

" 3. That, whereas in the case of the arsenobenzol compound the trypanocidal titre exhibited by the serum $2\frac{1}{2}$ minutes after intravenous injection approximated fairly closely to the calculated value, in the case of the other two compounds the titres observed were only small fractions of the calculated values."

The authors asked themselves :—

" Why in the case of N.A.B. does the titre observed $2\frac{1}{2}$ minutes after injection approximate to the calculated titre, whilst in the case of reduced tryparsamide thioglycollate it is only a small fraction of the calculated value ; . . . why during the hours which follow the injection does the titre fall so much more rapidly in the case of reduced tryparsamide than in that of novarsenobillon ? . . . Why . . . should the titre observed $2\frac{1}{2}$ minutes after intravenous injection of tryparsamide prove to be only a small fraction of the calculated value, and why should the titre rise during the next 6 hours instead of falling as in the case of the other compounds ? "

The experiments were designed to answer these questions and had the results described in the summary, given here in part.

" It was found that, if red cells were suspended at 37°C . in a solution of reduced tryparsamide in either Ringer-glucose or ' nutrient medium,' a certain amount of the drug rapidly passed into the red cells. This was evident from the fact that when these red cells were laked, after separation from the drug solution and washing rapidly in large volumes of iced saline, the laked solution was powerfully trypanocidal. Furthermore, when drug-laden red cells, washed in iced saline, were subsequently suspended in Ringer-glucose or ' medium,' drug diffused out of the red cells into the surrounding fluid.

" The amount of reduced tryparsamide which diffused into red cells depended firstly on the concentration of the drug in the surrounding medium, and secondly, although to a much less extent, on the length of time the red cells were exposed to the solution of drug. When red cells were suspended for 15 minutes at 37°C . in an equal volume of Ringer-glucose-drug solution containing 1 : 25,000 reduced tryparsamide, the concentration of drug within them was found to be $1/4\text{th}$ to $1/8\text{th}$ of that in the surrounding fluid ; when the concentration of the drug was increased 16 times, *i.e.*, to 1 : 1,562.5, the concentration found in the red cells was about $1/16\text{th}$ of that of the surrounding fluid. The amount of drug which had diffused into the red cells within 24 hours was in each case about double that found within 15 minutes. It was immaterial whether the drug was dissolved in Ringer-glucose alone or in ' nutrient medium ' (equal parts of Ringer-glucose solution and rabbit serum heated to 64°C . for 30 minutes)."

" Similar experiments on the diffusibility into red cells of the pentavalent compound tryparsamide gave more complicated results. Whilst

there seemed to be no doubt that tryparsamide, like its reduced homologue, diffused readily into red cells, it became at once obvious that another factor was at work which largely obscured the main issue. When red cells, which had been in contact for some hours with 0.5 per cent. solution of tryparsamide, and then washed thoroughly in iced saline, were suspended in drug-free Ringer-glucose solution, a substance was found to have diffused out of the red cells which was of enormously greater trypanocidal power than the 0.5 per cent. solution of tryparsamide. It is, therefore, clear that red cells are, in some way, able to change the relatively inert tryparsamide into a highly trypanocidal substance.

"This recalls certain interesting observations made many years ago by Levaditi, Yamanouchi and others. Levaditi and Yamanouchi (1908) showed that emulsions of liver, muscle and lung incubated with atoxyl transformed it into a trypanocidal substance which they termed 'trypanotoxyl'. . . . Yamanouchi (1910) considered that the trypanocidal substance was produced by the red cells; he found that liver and other organs cleared of blood no longer possessed the power of activating atoxyl. Yamanouchi further observed that red cells acted more powerfully in the presence of carbon dioxide than under normal conditions, and that in the presence of oxygen they failed altogether to activate atoxyl; pure recrystallized haemoglobin was without action. The active substance was soluble in alcohol, thermostable, and free from protein material. Terry (1912) found that both liver and blood, when incubated with atoxyl, transformed the drug into a toxic substance. The transforming agent in liver had, however, characteristics which, in some respects, were quite different from those of the active agent in blood. . . . In a later paper (1915), Terry showed that the toxic substance into which atoxyl is transformed (transformed atoxyl) is thermostable, but that the transforming agent in blood is thermolabile."

"We have concerned ourselves with a preliminary inquiry regarding the constituent of the red cell which is capable of increasing the trypanocidal power of pentavalent arsenicals.

"Our experiments showed that a solution of laked red cells was also able to activate tryparsamide in a similar degree to intact red cells. The extent to which a solution of red cells can activate tryparsamide is exceedingly great, as is shown by the following observation. The trypanocidal titre of a 1 per cent. solution of tryparsamide in 'medium,' either freshly-made or kept for 6 hours at 37°C., is 8; the trypanocidal titre of a 1 per cent. solution of tryparsamide in a 12.5 per cent. solution of red cells which has been kept for 6 hours at 37°C. is about 16,000; thus, by substituting the red cell solution for 'medium,' the trypanocidal titre is increased no less than 2,000 times.

"We do not know what constituent of the blood is responsible for producing this change. It cannot be haemoglobin itself since solutions prepared from pure crystalline haemoglobin showed no power to activate tryparsamide; and, furthermore, no differences were observed whether the haemoglobin was in the form of oxyhaemoglobin, reduced haemoglobin or carboxyhaemoglobin.

"Whatever its nature, the activating substance is relatively thermostable in that it resists almost completely a temperature of 65°C. for 30 minutes, and is not completely destroyed by a temperature of 75°C. for 30 minutes. The activating power of red cell solutions kept at 0°C. is gradually lost, so that, within two months or less, such solutions have become practically inert."

A. G. B.

STRANGEWAYS (Winifred I.). **Trypanocidal Action of Two Arsenicals, K. 324 and K. 352, on Infections in Mice and Rabbits.**—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 231–254.

This paper describes the trypanocidal action of two new aromatic arsenical compounds prepared by Dr. KING. The compounds are :—

K. 324. Di (β -carboxy- β -aminoethyl) benzamide-p-thioarsinite and K. 352. Di glutathionyl-4-acetamino-2-hydroxyphenyl thioarsinite. The tests were carried out on various trypanosomal infections in mice and rabbits. In order to control the investigation, parallel tests were made with tryparsamide.

Toxicity tests on mice were made with single intravenous injections. The mice were kept under observation for one month after treatment. It was found that the maximum dose which could be given to mice in a single intravenous injection was 0.075 mgm. per gm. of K. 324; 0.2 mgm. per gm. of K. 352; and 3.0 to 3.5 mgm. per gm. of tryparsamide.

The therapeutic values of the two drugs were tested on infections produced in mice by 5 different species of trypanosomes: (a) rapidly fatal infections due to *T. equiperdum*, *T. rhodesiense* and *T. brucei*, and (b) chronic infections due to *T. gambiense* and *T. congolense*. The results obtained with the acute infections are summarized in the following table which gives the approximate dose of each compound which produced 80 per cent. or more of cures, and also the therapeutic index, i.e., the ratio of the minimum curative dose (M.C.D.) to the maximum tolerated dose.

Drug	<i>T. equiperdum</i> M.C.D. (mgm. per gm.)	<i>T. rhodesiense</i> M.C.D. (mgm. per gm.)	<i>T. brucei</i> M.C.D. (mgm. per gm.)
K. 324	0.015-0.025 (1 = 1/3.75)	0.01 (1 = 1/7.5)	0.0075 (1 = 1/10)
K. 352	0.02 (1 = 1/10)	0.01 (1 = 1/20)	0.01 (1 = 1/20)

It is clear from this table that the two compounds provide an efficient means of curing the 3 infections in mice. The strain of *T. brucei* was most easily cured, that of *T. rhodesiense* rather less so, while *T. equiperdum* required relatively large doses.

The strain of *T. gambiense* used in these experiments was obtained from a patient in Entebbe in 1931. Its virulence for mice varied a good deal, some animals dying within the comparatively short period of a month, whereas others lived for as long as 8 or 9 months without showing any signs of infection after the first week. At first these mice were discarded as spontaneous cures, but more recently this was found to be a false assumption, and it now seems probable that the choroid plexus is a seat of *T. gambiense* in mice, and that animals can harbour the trypanosomes here without showing any signs of disease. In view of the chronic character of the untreated infections, it was necessary to keep the experimental mice under observation for as long as possible. It was found that doses of 0.01 mgm. per gm. of either K. 324 or K. 352, and 0.75 mgm. per gm. of tryparsamide sufficed to clear the peripheral blood of *T. gambiense* infections for long periods. Relapses were common after treatment with half the above dose of either K. 324 and K. 352. As might be expected neither drug had any curative action on *T. congolense* infections in mice.

A long series of therapeutic experiments were undertaken on rabbits infected with the strain of *T. rhodesiense*. The drugs were given intravenously 20 to 25 days after the inoculation of trypanosomes. At this time there were pronounced oedematous lesions of the ears and eye-lids as well as of the external genitalia, and trypanosomes could readily be found either in the peripheral circulation or in the fluid from the lesions. Results are given of two types of treatment with each drug, viz.: single injections of small or large doses, and repeated injections of small doses. It was found that single doses of K. 324 up to 0.02 gm. per kilo can be administered with safety to rabbits infected with *T. rhodesiense*, and that permanent cures can be produced with doses of 0.015 and 0.02 gm. per kilo. Short courses of treatment consisting of 3 to 6 doses of 0.01 gm. per kilo. produced permanent cures in rabbits infected with *T. rhodesiense*, and longer courses of treatment with the same dose produced no toxic symptoms in normal rabbits.

Single doses of K. 352 up to 0.04 gm. per kilo. could be safely administered to rabbits infected with *T. rhodesiense*, and permanent cures were produced by 0.02 to 0.04 gm. per kilo. Short courses of treatment with 4 to 8 doses of 0.01 gm. per kilo. of K. 352 produced permanent cures, whilst longer courses of treatment with the same drug produced no toxic symptoms in normal rabbits.

The following summary is given:—

"1. The two aromatic thioarsinites K. 324 and K. 352 are effective in curing *T. equiperdum*, *T. rhodesiense*, *T. brucei* and *T. gambiense* infections in mice in doses which are only a fraction of the maximum tolerated.

"2. Neither compound has any effect on *T. congolense* infections in mice.

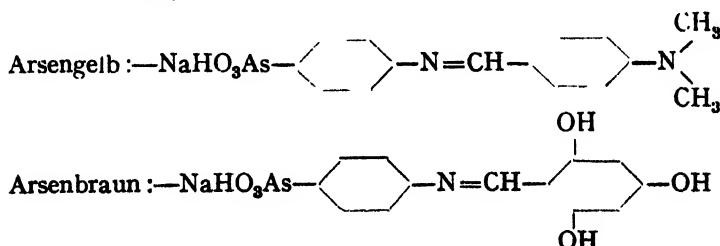
"3. Rabbits infected with *T. rhodesiense* can be cured with single intravenous doses of both compounds, but more effectively by a short course of 3 to 8 smaller doses.

"4. The relatively small amount of arsenic required to effect permanent cures in rabbits infected with *T. rhodesiense* when administered as the two thioarsinites, compared with that required when given as an arsonic acid such as tryparsamide, is discussed."

W. Y.

FISCHL (Viktor) & SINGER (Ernst). Chemotherapeutische Prüfung zweier arsenhaltiger Farbstoffe. [The Chemotherapeutic Examination of Two Arsenic-containing Dyes.]—*Biochem. Ztschr.* 1935. Feb. 22. Vol. 276. No. 4. pp. 277-279. [10 refs.]

The action of two arsenic containing dyes was tested on mice infected with nagana and *Sp. recurrentis*, respectively. The dyes in question are referred to as "Arsengelb" and "Arsenbraun"; they have the following formulae:—



It was found that both, especially the "Arsenbraun," were active on the trypanosome infection, and that "Arsenbraun" was also active on the spirochaete infection. W. Y.

FISCHL (Viktor). Chemotherapeutische Prüfung einiger Pyrrolfarbstoffe. [**Chemotherapeutic Examination of Some Pyrrol Dyes.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. May 29. Vol. 85. No. 1/2. pp. 77-80. [10 refs.]

WREDE and HETTICHE have recently obtained from cultures of *Bacillus prodigiosus* a red dye, Prodigiosin, and Fischl has examined the therapeutic value of the perchlorate of this substance. He found that a suspension in almond oil given subcutaneously to mice infected with nagana caused the temporary disappearance of the trypanosomes. Three other pyrrol dyes—pyrrolblue, pyrrolred, and phtalocyanin—had no trypanocidal action. W. Y.

V. JANCsó (N.) & V. JANCsó (H.). Chemotherapeutische Mittel mit opsoninartiger Wirkung. [**Chemotherapeutic Drugs with an Opsonic Action.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Apr. 29. Vol. 84. No. 5/6. pp. 471-504. With 1 fig. [16 refs.]

The authors discuss in detail their investigations on the opsonic action of certain drugs. As they have recorded in various earlier papers [*ante*, pp. 22 and 358] they have observed that the intravenous injection of an electro-colloidal copper preparation, in combination with splenectomy, completely prevents the phagocytosis of foreign particles or micro-organisms from the circulation, owing to an efficient elimination of the reticulo-endothelial system. This new technique has shown that phagocytosis and opsonic action plays just as important a part in chemotherapy as in immunology.

When animals experimentally infected with trypanosomes are treated with germanin the reticulo-endothelial cells of the liver, spleen and bone-marrow exhibit an enormous phagocytosis of flagellates, and this is dependent upon the opsonizing action of the drug. In other experiments trypanosomes were subjected to the action of germanin *in vitro*, and then equal numbers were injected into mice with an intact reticulo-endothelial system, and into mice which had been splenectomized and treated with electro-colloidal copper. In this way it was shown that the cells of the reticulo-endothelial system were able to phagocytose and destroy millions of living trypanosomes.

The preparation of trypanosomes for phagocytosis was not brought about only by germanin, but also by withdrawal of sugar. When trypanosomes suspended in a nutrient medium have exhausted the glucose content of the medium they become motionless, and in this condition of "sugar hunger" they are avirulent and become a ready prey to the reticulo-endothelium by which they are phagocytosed and destroyed. The addition of fresh serum or glucose, however, restores the virulence of the parasites. If trypanosomes in a condition of "sugar hunger" are injected intravenously into a normal mouse they are phagocytosed by the reticulo-endothelial cells to the extent of many millions within a few minutes. Experimental investigations have suggested that the basis of the action of germanin is a toxic

inhibition of the sugar metabolism of the trypanosomes, and consequently it is possible that the opsonic effect of the drug depends upon this action. This hypothesis is in harmony with the fact that trypanosomes obtained from an animal which has been given a dose of germanin consume less oxygen and sugar than do trypanosomes from an untreated animal.

The very interesting fact was discovered that whereas a normal strain of *T. brucei* when suspended in a solution of germanin for 30 minutes at 37°C. failed to bind the drug, nevertheless its trypaflavin-fast branch completely lost its virulence after similar treatment. It appears therefore that systematic treatment of a trypanosome strain with trypaflavin increases the permeability of the trypanosomes for germanin. This observation explains the synergism between trypaflavin and germanin.

W. Y.

SINGER (Ernst) & FISCHL (Viktor). Arzneifestigkeit und Chemikalingewöhnung der Trypanosomen. [**Drug-Resistance and Chemical Habituation of Trypanosomes.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1935. Feb. 25. Vol. 116. No. 6. pp. 683-687.

In previous papers the authors have put forward the view that although absorption of a drug by the parasite is necessary for chemotherapeutic action, it is not necessarily identical with this. They have shown that such drugs as atebrian and rivanol, which have no trypanocidal action, are just as readily absorbed by trypanosomes as is the trypanocidal dye trypaflavine.

It has now been established that when trypanosomes are exposed for some time to the action of trypanocidal substances, such as trypaflavine, a state of affairs is gradually reached in which the parasites no longer absorb the drug. It occurred to the authors that it would be interesting to ascertain what happened when trypanosomes were repeatedly exposed to the action of such non-trypanocidal substances as atebrian and rivanol. In striking contrast to what happens in the case of trypaflavine, it was found that trypanosomes, which had been subject to the action of the non-trypanocidal compounds during 12 passages through mice, instead of absorbing less of these dyes than the normal strain were capable of absorbing $2\frac{1}{2}$ times as much.

From this work it is concluded that chemical habituation is fundamentally different from drug-resistance. Systematic treatment of *T. lewisi*, which possesses a natural resistance to arsenicals, with solu-salvarsan, failed to influence the capacity of the trypanosomes to absorb the drug in either a positive or a negative direction.

W. Y.

VON JANCsó (Nikolaus) & VON JANCsó (Hertha). **The Rôle of the Natural Defence Forces in the Evolution of the Drug-Resistance of Trypanosomes. II.—The Rapid Production of Germanin-fast *T. brucei* Strains in Animals with Paralyzed Defence.**—*Ann. Trop. Med. & Parasit.* 1935. Apr. 25. Vol. 29. No. 1. pp. 95-109. With 1 fig. [21 refs.]

A description is given of a rapid method of producing germanin-fast strains of trypanosomes. The method consists essentially in eliminating the reticulo-endothelial system in mice, firstly by splenectomy 2 to 4 hours before treatment, and secondly by the intravenous injection of electro-colloidal copper 3 to 4 hours after the injection of germanin.

It was found that when mice infected with *T. brucei* were treated in this manner, a drug-fast strain of trypanosomes was obtained with remarkable rapidity. After 12 treatments in the "blocked" animals the trypanosomes were found to withstand the "dosis bene tolerata," i.e., 1/200 gm. of germanin per 20 gm. mouse. This is in striking contrast with the attempts to produce a germanin-fast strain in the ordinary way.

The reviewer and his colleagues record that 12 months were required to make a strain of *T. rhodesiense* completely resistant to germanin; and LEUPOLD, who worked with the same strain as von Jancsó, records that maximal resistance to germanin was not obtained until after 100 passages.

von Jancsó considers that the most plausible explanation of this interesting phenomenon is that trypanosomes possess a capacity for adapting themselves very quickly to germanin, and that normally a rapid production of drug-fastness does not take place because the defence forces of the host (that is the reticulo-endothelial system) counteract the tendency to its production. W. Y.

VON JANCÓS (N.) & VON JANCÓS (H.). Chemotherapeutische Schnellfestigung von Trypanosomen durch Ausschaltung der natürlichen Abwehrkräfte. [**Rapid Production of Drug-fast Strains through Elimination of the Natural Defence Mechanism.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. May 29. Vol. 85. No. 1/2. pp. 81-105. With 1 fig. [27 refs.]

Reference is made to the rapid production of germanin-resistant trypanosomes by the treatment of infected mice in which the reticulo-endothelial system is eliminated by splenectomy and intravenous injection of electro-colloidal copper. This experimental work has already been published elsewhere and noticed in this *Bulletin* [ante, p. 22 and p. 358]. [The paper is of a highly technical nature dealing with various problems on the subject of drug-resistance; it should be consulted in the original by those interested.] W. Y.

SCHLOSSBERGER (H.) & SCHÜFFNER (R.). Festigungsversuche an Trypanosomen mit Arsenpyridinderivaten. [**Experiments on Resistance in Trypanosomes with Arseno-Pyridine Derivatives.**—Reprinted from *Angewandte Chemie*. 1934. Vol. 47. p. 768 in *Arb. a. d. Reichsgesundheitsamt*. 1935. Feb. Vol. 67. No. 4. pp. 577-584. [19 refs.]

Experiments were devised with the object of ascertaining whether trypanocidal arsenical derivatives of heterocyclic compounds, particularly of pyridine, are capable of a therapeutic effect upon trypanosomes rendered resistant to a phenylarsonic acid preparation, and whether trypanosomes resistant to an arsenopyridine compound can be influenced by a phenylarsonic preparation.

The experiments were made on *T. brucei* infections in mice. Two resistant varieties of the strain, viz.: one resistant to tryparsamide, and the other to the preparation BRI (i.e., mono-sodium salt of 2-pyridone 5-arsonic acid) were prepared in the usual way. The minimum therapeutic dose of each of a large number of preparations was determined on infections produced by the normal and by the two resistant strains. The preparations used included tryparsamide

and BR1, a number of arsenopyridine compounds, viz.: BR20, BR23, BR120, BR121, and also arsenophenylglycine, an arsenostibino-benzene derivative (Sdt 355), trypanflavine, germanin, tartar emetic and fuadin. The results of the experiments are given in detail in tabular form. They show that the strain made resistant to the arsenopyridine compound, BR1, was resistant not only to the other arsenopyridine derivatives, but also to trypanamide, trypanflavine and fuadin. The trypanamide-resistant strain, however, proved sensitive to BR1, and particularly so to BR23 and to fuadin.

These observations can be explained only on the assumption that the mechanism of action of both pyridine derivatives (BR1 and BR23) differs from that of trypanamide and from that of the phenylarsonic derivatives. These results resemble those of EHRlich in the course of his investigations on drug-resistance whilst studying arsenophenylglycine, results later confirmed by the reviewer and his colleagues.

The conclusion seems justified that, similarly to arsenophenylglycine, the arsenopyridine preparations BR1 and BR23 possess affinities to the protoplasm of the trypanosomes which trypanamide and other derivatives of phenylarsonic acid do not have. Since, however, the BR1-resistant strain can be appreciably affected by arsenophenylglycine, the anchoring points of arsenopyridine compounds must partly differ from those of arsenophenylglycine. In terms of EHRlich's chemoreceptor theory, it would appear that the two arsenopyridines possess "secondary haptophors," just as does arsenophenylglycine, but that they are different from those of arsenophenylglycine. From the practical point of view, these conclusions are important, because they indicate possibilities of cure in cases where organisms resistant to trypanamide, atoxyl, etc., are involved.

W. Y.

BROWNING (C. H.) & GULBRANSEN (R.). **Variation in Chemotherapeutic Susceptibility associated with Change in Virulence of a Strain of *Trypanosoma brucei*.**—*Jl. Hygiene*. 1935. May. Vol. 35. No. 2. pp. 180-184.

A strain of *T. brucei* when first introduced into mice produced infections relatively resistant to various drugs, but when the strain had become highly accommodated, and its pathogenicity increased to a maximum as the result of repeated passages, the infected mice were readily cured.

The strain of *T. brucei* used in these experiments was obtained by ADAMS from a dog which had been exposed to the bites of wild fly in Uganda. It was preserved by passage through six guineapigs during the course of 8 months, and thereafter maintained by passage through mice. Up to the 12th passage most of the mice showed a marked fluctuation in the number of parasites in the blood before death finally took place when they were numerous. This fluctuation, as well as the length of survival, are better indications of the state of accommodation of the trypanosomes than is the incubation period. From the 14th passage onwards the strain possessed nearly the maximal pathogenicity, and the parasites appearing in the blood increased progressively until death, which in all animals, except one in the 18th passage, occurred within 3 days thereafter. The strain, therefore, accommodated itself fairly rapidly to the mouse.

Therapeutic tests with various trypanocidal substances were carried out during the early passages (1 to 8) and also during later passages

(34 to 290). The results, which are summarized in a table, showed that the infection at first was markedly resistant to all the substances tested, viz.: arsacetin, tryparsamide, trypanblue, Bayer 205, trypanflavine, and styryl-quinoline compounds. Animals of the later passages were, however, for the most part cured by the same or smaller doses of these drugs.

The exact mechanism on which this difference depends was not investigated, but attention is drawn to the interesting fact that chemotherapeutic response was weak at the time when the host itself was able to exercise an effective resistance, and that later, when the host's resistance had become negligible, the curative action of the drugs was pronounced.

W. Y.

BROWNING (C. H.) & GULBRANSEN (R.). **Combined Treatment of Experimental Trypanosome Infections by Chemotherapeutic Agents.** —*Jl. Path. & Bact.* 1935. May. Vol. 40. No. 3. pp. 425-431. [25 refs.]

Experiments showed that combined therapy in which tryparsamide and styryl-245 were used in sequence produced a greater curative effect in mice infected with *T. brucei* than followed the use of large doses of either substance alone.

The results of the experiments are set out in a series of tables. It was found that of the mice treated with tryparsamide alone, all those which were given a dose of 1 : 400 or less relapsed, as did one of the two mice which received a dose of 1 : 150. In the case of treatment with styryl-245 alone considerable variation in action was seen, thus 1 : 2,000 did not invariably lead to cure, whilst 1 : 24,000 produced cure in a few cases. With doses of 1 : 2,000 to 1 : 5,000, 10 of 23 animals were cured, whilst with doses of 1 : 20,000 to 1 : 30,000 only one of 23 mice was cured.

Where tryparsamide and styryl-245 were used jointly, 1 : 250 to 1 : 400 of the arsenical and 1 : 7,500 to 1 : 18,000 of the styryl compound produced a cure in all of 17 animals; whilst tryparsamide 1 : 400 with 1 : 24,000 to 1 : 30,000 of styryl cured 17 of 33 mice.

The authors believe that the evidence is strongly in favour of this result being more than a mere summation of effects. It is left undecided how exactly this "potentiation" or "synergic" action is produced, but it is emphasized that tryparsamide is quickly absorbed and excreted, whereas the styryl compound is slowly absorbed and acts gradually. The advantage of combined treatment in this particular instance may be due to the prolonged influence of the styryl compound on parasites weakened by the arsenic, as well as to the fact that the substances differ widely in chemical constitution and so are likely to attack the parasites at different points.

W. Y.

- i. HASSKO (A.). Experimentelle Beiträge zur Wirkungsweise chemotherapeutischer Mittel I. [**The Mode of Action of Chemotherapeutic Substances.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1935. Feb. 25. Vol. 116. No. 6. pp. 660-668. [11 refs.]
 - ii. —. Untersuchungen ueber den Wirkungsantagonismus chemotherapeutischer Mittel II. [**The Antagonistic Action of Chemotherapeutic Substances.**]—*Ibid.* pp. 669-671.
- i. The experiments described in this paper were devised with the object of ascertaining something about the mechanism of action of

certain drugs, *e.g.*, parafochsin, trypanflavine and neosalvarsan, on trypanosomes, and especially whether their action was direct.

Rats were inoculated with a strain of nagana very sensitive to trypanflavine and salvarsan, and at the height of the infection were treated with one or other of the three drugs in question. At various intervals afterwards the animals were killed by bleeding and the trypanosomes separated from the cellular elements of the blood by fractional centrifugation. The amount of dyestuff bound by the trypanosomes was estimated colorimetrically and the amount of neosalvarsan by chemical reagents. At various times after treatment the vitality of the parasites and their virulence were examined by subinoculation into mice.

It was found that when trypanosomes which had been treated with trypanflavine or neosalvarsan were subinoculated into normal mice multiplication of the parasites was delayed. Their infectivity was proportional to the dose and the therapeutic index of the drug, and to the time of its action. Trypanosomes treated with parafochsin were just as infective for normal mice as was the normal untreated strain. In tables the authors show the amount of parafochsin or trypanflavine found in the trypanosomes at various intervals after treatment of infected rats. Parafochsin showed less avidity for the parasites than did acriflavine; it was found that the trypanosomes took up 10 times as much acriflavine as parafochsin.

Neosalvarsan itself, however, could not be demonstrated in the trypanosome body. The authors therefore believe that the active agent must be formed by the body of the host from neosalvarsan and that this product, whatever it may be, acts directly on the parasites.

In further experiments it was noticed that blocking of the reticulo-endothelial system limited the action of tartar emetic, and the conclusion is reached that the function of this system is to remove damaged parasites by phagocytosis.

ii. Previous experiments had suggested that dyes belonging to the triphenylmethane series behave differently in trypanosome infections of rats and mice. For example, it is stated that brilliant green given to a nagana infected rat greatly interferes with the effectiveness of a subsequent dose of acriflavine, but that this does not happen with the same infection in white mice; and conversely previous treatment of infected rats with methyl- or ethyl-violet scarcely interferes with the action of acriflavine, but in mice exerts a definite antagonistic action.

The author determined to re-investigate these questions. A number of experiments were performed with white rats infected with a strain of nagana sensitive to the triphenylmethane dyes. The animals were given 5 mgm. per 100 gm. of either methyl violet, ethyl violet or pyoktanin, or 10 mgm. per 50 gm. of trypanrot or trypanblue. An hour later they were given subcutaneously 1 mgm. per 50 gm. of trypanflavine. After the lapse of a further hour the rats were killed by bleeding, the trypanosomes separated from the cellular elements of the blood, dried and weighed, and their content of dye or acriflavine determined. It was found that a preliminary dose of methyl violet, ethyl violet or pyoktanin greatly lessened the capacity of the trypanosomes to take up acriflavine, whilst the preliminary dose of trypanrot or trypanblue almost entirely prevented the absorption of acriflavine by the parasites.

W. Y.

LAUNOY (L.). De l'action synergique de l'arsenic et de l'antimoine dans le traitement du nagana expérimental de la souris. [**Synergic Action of Arsenic and Antimony in the Treatment of Experimental Nagana in Mice.**].—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 324-329.

It is well known that nagana in mice is very sensitive to arsenical compounds and to Bayer 205, but relatively resistant to antimony compounds. The author has asked himself whether it is possible to obtain any synergic action with a very active arsenical compound and a relatively inactive antimonial compound.

For his experimental work he selected orsanine as his arsenical preparation, and two compounds of antimony, viz.: antimony trithiosalicylate of sodium and antimony III-thiomalate of lithium. It was found that a dose of 3 mgm. of orsanine intravenously cured 100 per cent. of infected mice. The doses used in the synergic experiments were (a) Orsanine 1 mgm. and Sb. trithiosalicylate of sodium 0.5 mgm.; and (b) Orsanine 1 mgm. and Sb. thiomalate of lithium 1.4 mgm. to 1.8 mgm. It was found that this dose of orsanine alone cured only about 23 per cent. of animals. Of 35 mice treated with 0.5 mgm. of the first antimony compound, none were cured. Of 30 mice treated with 2.8 mgm. of the second antimony compound, 16 were sterilized and some died from poisoning. With the lower dose mentioned above only a few animals were sterilized. The results of the synergic experiments are as follows:—

The first pair of drugs given simultaneously in the doses mentioned cured 5 of 10 mice, and when given successively they cured 3 of 10. The second pair of drugs gave better results. When the dose of the antimony compound was 1.4 mgm. 7 of 10 mice were cured, and when the dose was 1.8 mgm. all the mice were cured. W. Y.

DUKE (H. Lyndhurst). **Arsenic Resistance in Trypanosomes.** [Correspondence].—*Lancet.* 1935. Apr. 13. pp. 903-904.

Duke complains that the reviewer and his colleague, Dr. MURGATROYD, in their recent Address to the Royal Society of Tropical Medicine on the subject of chemotherapy, omitted to refer to certain experiments performed by him in Uganda. [It was, of course, impossible, in the limited period available, to summarize the entire literature of chemotherapy, and reference was made to a few only of those articles which seemed to the reviewer and his colleagues to bear most directly on the various points discussed.] W. Y.

FISCHL (Viktor) & SINGER (Ernst). Die Chemotherapie der Ratten-trypanose. [**The Chemotherapy of Rat Trypanosomiasis.**].—*Ztschr. f. Hyg. u. Infektionskr.* 1935. Feb. 25. Vol. 116. No. 6. pp. 652-659. [43 refs.]

This work was undertaken with the object of throwing light on the mechanism of the action of chemotherapeutic substances on infections due to *Trypanosoma lewisi*.

Apart from arsenophenylglycin the only substances known to have any action on *T. lewisi* infections are BR23, Sdt. 355 and 386B (CHRISTISON) and, to a slight degree, atoxyl. The authors themselves have tried the effect of sodium arsenite, m-amino-p-oxyphenyl sodium arsenite, sodium salvarsan, solusalvarsan, sulfoharnstoff, ruthenrot, rhodium sodium chloride, trypaflavine and human serum. All these substances were found to be inactive. In a couple of tables are collected

the results obtained by various workers, and by the authors themselves, with these and many other substances on *T. lewisi* and related apathogenic trypanosomes.

In addition to its action on *T. lewisi* arsenophenylglycin exhibits another peculiarity, namely, that it can affect pathogenic trypanosomes which have been made resistant to other arsenicals; this property EHRLICH called "avidity." CHRISTISON explained this phenomenon on EHRLICH's hypothesis as follows:—Although *T. lewisi* and arsenic-fast nagana trypanosomes possess no arseno-receptors, they are provided with an acetico-receptor which is capable of anchoring arsenophenylglycin to their cytoplasm. The negative results of Christison with BR68, and of the authors with solusalvarsan, and the positive results of Christison with atoxyl, BR23 and Sdt. 386B show, however, that the acetic acid ester alone cannot explain the action on the apathogenic trypanosomes. It is still more difficult to explain on chemical constitution the activity of drugs on *T. lewisi* and arsenic-fast strains of pathogenic trypanosomes, respectively.

In order to throw light on the mechanism of action of chemotherapeutic substances on *T. lewisi*, the authors injected a series of rats in an early stage of infection with various substances, *e.g.*, arsenophenylglycin, atoxyl, sodium salvarsan, neosalvarsan, solusalvarsan, sodium arsenite, solganol and sulfoharnstoff. The animals were killed an hour later by bleeding and the amount of arsenic or gold determined in the plasma, red corpuscles and trypanosomes, respectively; the arsenic was estimated colorimetrically and the gold by a spectrographic method. The results are set out in a table from which it appears that trypanocidal action and anchoring of the drug are parallel; the active arsenophenylglycin is absorbed by the trypanosomes in considerable amount, whilst the slightly active atoxyl is absorbed in much smaller amount. The remaining inactive arsenicals were absorbed in very small amounts. The gold compounds—solganol and sulfoharnstoff—were, however, absorbed in considerable quantities notwithstanding their complete therapeutic inactivity.

These results show once more that absorption of a drug is not necessarily identical with curative effect; although absorption of a certain quantity of the drug is necessary for curative effect, the converse is not true; a considerable quantity of a drug can be absorbed without curative action.

W. Y.

CORSON (J. F.). **A High Rate of Salivary Gland Infection of *Glossina morsitans* with *Trypanosoma rhodesiense*.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 501–504.

After referring to the fact that in transmission experiments with *G. morsitans* and *T. rhodesiense* it is usual to obtain less than 10 per cent. of salivary gland infections, the author gives details of an experiment in which a very high proportion of such infections was obtained.

A reeduck was bought in the sleeping sickness-area of the Kahama District of Tanganyika in September, 1934. In 1928–1929 it was estimated by MACLEAN that the sleeping sickness in the particular district in which this reeduck was caught amounted to the unusually high figure of 22 per cent. The reeduck was taken to the Tinde Laboratory and remained in good health. Examinations of its blood and subinoculations into 9 white rats were negative. On Sept. 14th two isolated *G. morsitans* infected with *T. rhodesiense* were fed on the reeduck.

The history of the strain is as follows:—

24.7.33. Man—Guineapig 95—Fly 10—Dikdik 2—Fly K8—Dikdik 8—Fly S8—Dikdik 13—Fly AA53—Dikdik 19—Flies AI.27 and 41—Reedbuck. 14.9.34.

This strain was shown in August, September and October, 1934, to be infective for man. In transmission experiments from infected dikdiks by *G. morsitans* usually one or two infective flies out of about 20 to 40 survivors were isolated. On October 4th about 120 laboratory-bred *G. morsitans* were fed on the reedbuck, the blood of which showed a scanty infection of trypanosomes; the flies were again fed on Oct. 7th and another box of about 30 flies was added on this occasion. On this day only 3 trypanosomes were found during the examination of 3 thick films of the reedbuck's blood. The flies were then fed on a healthy sheep until Oct. 23rd, after which they were transferred to monkeys. When the monkeys became infected the 85 flies left were put singly into bottles, and each fly was allowed to bite a white rat; 47 rats became infected. Further animals were infected, and finally the flies were dissected and 46 showed infected salivary glands; including the flies which had infected rats, but which were not dissected, 51 (60 per cent.) of the 85 flies had infected salivary glands. The blood of the rats showed numerous posterior-nuclear forms, the incubation period was 45 days and the duration of life about 20 days. There was nothing unusual in the climatic conditions; the temperature of the air of the laboratory ranged daily from about 70–85°F., sometimes reaching 90°F. The flies were kept in boxes over water in trays, partly to keep the air moist and partly to guard against white ants.

A similar experiment with the same strain of trypanosomes in a dikdik, and with flies from the same batches of pupae, ran concurrently with the reedbuck experiment; in this, although the infection was transmitted to a monkey and 32 flies survived to feed singly on rats, an infective fly was not isolated.

In view of these remarkable results, it appeared desirable to repeat the experiment accompanied by some form of control. In the second experiment 120 *G. morsitans* were fed on the same reedbuck on the 9th and 12th November. On the 6th December, the surviving flies were dissected and 28 (33.3 per cent.) of the 84 surviving flies were found to have infected salivary glands.

In the control experiment a few of the isolated flies infected in the original experiment were allowed to bite a monkey on the 8th November. This monkey became infected and 120 *G. morsitans* were fed on it on the 13th, 14th and 15th November. The rate of infection of the salivary glands in this experiment was only 1.1 per cent. In Corson's opinion the special suitability of the reedbuck's blood rather than a selective change in the trypanosomes appears to be the most likely explanation of this interesting observation. W. Y.

CORSON (J. F.). Further Observations on Francolin and Guinea-Fowl as Reservoirs of *Trypanosoma rhodesiense*.—*Jl. Trop. Med. & Hyg.* 1935. Feb. 15. Vol. 38. No. 4. pp. 46–47.

In previous papers it was shown that francolin and guinea-fowl were susceptible to infection with *T. rhodesiense* [this *Bulletin*, Vol. 29, p. 635]. In his present work Corson has firstly attempted to infect these birds by allowing isolated infected *G. morsitans* to feed upon them, and secondly he has endeavoured to ascertain whether guinea-fowl in an evacuated sleeping sickness area are infected by inoculation of their blood into rats.

In the first portion of his work Corson used a strain of *T. rhodesiense* isolated from man in July, 1933, and since maintained by passage through *G. morsitans* and dik-diks. A bottle containing the infected fly was applied to the leg of the bird until the fly bit or fed. Rats were subsequently inoculated from the birds and laboratory-bred flies fed on those birds which had been shown to be infected. Details of the successful experiments are given in a table. Three of the 19 francolin and 3 of the 9 guinea-fowl became infective to rats. One francolin remained infective for 3 months and 1 guineapig for 18 days, but not for 2 months. Several hundred laboratory-bred *G. morsitans* were fed on the infected birds, but the infection was not transmitted.

The second group of experiments was performed at Mkwemi in the Kahama district. The population had been evacuated in 1928, because of sleeping sickness. Tsetse and antelope are plentiful. In all, 134 rats were inoculated from 67 guinea-fowl, but none became infected.

Corson concludes from this and his previous work that francolins and guinea-fowl, like the domestic fowl, need not be considered as more than, at most, very rare and temporary reservoirs of *T. rhodesiense*.

W. Y.

PACKCHANIAN (Ardzroony). **A Method of maintaining Laboratory Strains of *Trypanosoma brucei* in a Subspecies of *Peromyscus maniculatus*.**—*Jl. Lab. & Clin. Med.* 1935. Feb. Vol. 20. No. 5. pp. 510-515. With 2 charts. [11 refs.]

The author suggests the use of an American deer mouse, viz.: a sub-species of *Peromyscus maniculatus*, as a suitable laboratory animal for maintaining parasitic strains of *T. brucei*, *T. equiperdum* and *T. evansi*. In comparison with the procedure usually adopted of maintaining these trypanosomes in rats, mice and guineapigs, the method recommended is both inexpensive and time-saving.

When *P. maniculatus* is inoculated intraperitoneally with *T. brucei*, the parasites appear in the circulation in 2 or 3 days; they gradually increase until they are very numerous, and then they more or less suddenly disappear from the circulation. The first crisis and the subsequent short latent period are followed by a relapse, the parasites steadily increasing in number until they are swarming. Occasionally the animal dies at this stage, but more commonly there is a series of crises and relapses.

In the author's experiments, it was found that the minimum period of life of *P. maniculatus* infected with the laboratory strains of *T. brucei* and *T. evansi* was 21 days, the maximum period was 230 days, and the average about 80 days. There was no evidence that the sojourn of the parasites in this host caused any attenuation in their pathogenicity for ordinary laboratory animals.

W. Y.

VAN DEN BRANDEN (F.). Pouvoir infectant du sang de rats albinos, après injection sous-cutanée massive de *Trypanosoma congolense* et de *Trypanosoma brucei*. [**Infectivity of the Blood of Albino Rats after Massive Subcutaneous Injection of *T. congolense* and *T. brucei*.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 14. pp. 1479-1481.

The author objects to the modification of the term "incubation" suggested by VALENZA (1934-35), who distinguishes between what he calls bacteriological incubation and clinical incubation.

He performed a series of experiments in which rats were inoculated subcutaneously with *T. congolense* or *T. brucei*. These strains were both very virulent, killing the rats in 6 to 8 days, the trypanosomes appearing in the blood in 4 or 5 days. An albino rat weighing 100 to 120 gm. was then given subcutaneously 1 cc. of blood rich in trypanosomes: an hour later the heart was punctured and 1 cc. of blood removed added to 0.25 cc. of 6 per cent. citrate solution and injected subcutaneously into a healthy rat. This animal showed trypanosomes in its blood 4 to 5 days after the inoculation. Blood removed from the heart of the first rat 36 to 48 hours after infection was likewise infective for healthy rats, but the incubation period was prolonged for a couple of days. From this it is concluded that after a massive injection of trypanosomes the parasites are soon found in the circulation in considerable numbers, but later on (between the 36th and 48th hours) they are caught up in the deep organs; and finally they overflow into the blood. This experiment was repeated many times, both with *T. congolense* and *T. brucei*, and the results were always the same. In conclusion van den Branden writes that it is very desirable, in medicine and in natural science, to avoid modification of common terms which are consecrated both by time and by tradition. W. Y.

VAN DEN BRANDEN (F.). Sur le rapport du poids de la rate ou du foie au poids du corps, chez des rats blancs (variété albinos de *Mus decumanus*), non infectés, ainsi que chez les animaux de même espèce, préalablement infectés de *Trypanosoma congolense* ou de *Trypanosoma brucei*, puis guéris ou non guéris par traitement. [The Relationship of the Weights of the Spleen or of the Liver to the Weight of the Body in Normal White Rats and in those Infected with *T. congolense* or *T. brucei*, and Subsequently either Cured or Not Cured by Treatment.]-C. R. Soc. Biol. 1935. Vol. 119. No. 20. pp. 529-530.

VALENZA, in a recent paper, has drawn attention to the considerable enlargement of the spleen in certain animals infected with *T. congolense*, and has inquired whether the weight of the spleen in treated mice would not provide useful indications concerning the course of the infection and proof of cure. He concluded from his work that hypertrophy or non-hypertrophy of the spleen was a satisfactory indication of cure or non-cure of treated animals. VALENZA used the formula $PR/PC \times 100$, where PR represents the weight of the spleen and PC the weight of the body.

Van den Branden has repeated this work, using white rats infected with *T. brucei* or *T. congolense*, and in addition has investigated the variation in the weight of the liver. In normal rats he found $PR/PC \times 100$ varied between 0.4 and 0.6, whereas the formula $PF/PC \times 100$ was on an average 5. In rats infected with *T. congolense* $PR/PC \times 100$ varied between 1.0 and 3.0, and $PF/PC \times 100$ averaged 5. In rats infected with *T. brucei* the figures were approximately the same.

The conclusion reached, therefore, is that the spleen is greatly hypertrophied in rats infected with *T. congolense* or *T. brucei*, whereas the weight of the liver remains normal. Histological examination of the hypertrophied spleen showed that the enlargement was due to a great increase in the reticulo-endothelial system.

In rats infected with *T. congolense* or *T. brucei*, and subsequently cured by a trivalent antimonial, the formulae were practically identical

with those given by normal animals ; whereas in rats unsuccessfully treated the formula $PR/PC \times 100$ gave a value of 1.0 or more.

Van den Branden's work, therefore, confirms VALENZA's hypothesis, namely, that the presence or absence of splenic hypertrophy affords indication of cure or non-cure. W. Y.

VALENZA (J.). Maladies expérimentales de réinfection. [**Experimental Re-infection.**].—*Arch. Inst. Pasteur de Tunis*. 1935. Jan. Vol. 24. No. 1. pp. 92-98.

In his work on the therapy of *T. congolense*, the author found that a certain number of guineapigs infected with this parasite were cured either by moranyl alone or by this drug in combination with tryparamide or with Sb-111-thiomalate of sodium. The object of the present experiment was to determine whether the animals thus cured were immune to a new infection with the same parasite.

The general conclusion to be drawn from this investigation is that the cured animals are not immune to re-infection ; but it was observed that in certain cases the second infection was manifested only by a rise of temperature, the blood remaining negative and not infecting a fresh animal. A second re-infection always succeeded, and this suggests that the first re-infection had exhausted the antibodies circulating in the blood. W. Y.

TSENG (Hsienli). Ueber die gegenseitige Beeinflussung verschiedener Trypanosomen bei Mischinfektion. [**On the Reciprocal Influence of Different Trypanosomes in Mixed Infections.**].—*Zent. f. Bakt.* I. Abt. Orig. 1935. June 14. Vol. 134. No. 3/4. pp. 153-159.

It has long been known that different species of bacteria may, in mixed infections, exert an antagonistic action on one another ; but little is known about the antagonistic action of different species of protozoa, and it was with the object of investigating this problem that the experiments described in the present paper were undertaken.

The author used young rats and mice, and species of trypanosomes which were morphologically easily distinguishable from one another, viz. : *T. congolense*, *T. gambiense* or *T. brucei*, *T. lewisi* and *T. cruzi*. In pure infections it was found that *T. gambiense*, *T. lewisi* and *T. cruzi* appeared in the blood in about 4 to 6 days, whilst *T. congolense* and *T. brucei* appeared within 1 or 2 days. Infections with the last two trypanosomes were rapidly fatal ; the other infections ran a chronic course.

Mixed infections with *T. gambiense*, *T. lewisi* and *T. cruzi* produced no definite result. Very different, however, was the case in another set of experiments in which the mixed infections consisted of *T. congolense*, *T. brucei* and *T. cruzi*. In this series of experiments, *T. brucei* completely inhibited the development not only of *T. cruzi*, but also of *T. congolense*. In order to investigate this interesting phenomenon more carefully, a number of rats were inoculated with *T. congolense*, and when this parasite was present in the blood 3 days later, the animals were also inoculated with *T. brucei*. The results, which are set forth in a table, show that the *congolense* infection waned as the *brucei* infection waxed. Somewhat similar results were obtained with mice, and the general conclusion drawn is that *T. brucei* infections are antagonistic to *T. congolense*. W. Y.

- SCHILLING (Claus). Immunisierung gegen Trypanosomenkrankheiten. [Immunization against Trypanosomiasis.]—*Deut. Med. Woch.* 1935. May 24. Vol. 61. No. 21. pp. 832-834.
- . Immunization against Trypanosomiasis.—*Jl. Trop. Med. & Hyg.* 1935. May 1. Vol. 38. No. 9. pp. 106-108.

The author has continued in Tanganyika his work on immunization against trypanosomiasis [this *Bulletin*, Vol. 31, p. 213]. As mentioned in his earlier papers, it is essential that immunization is performed on quite young animals, and accordingly in the present work he has used young calves, since foals do not exist in the part of Africa in which he was working, *e.g.*, Tinde. Of the three species of trypanosomes found in Tanganyika, *T. congolense*, *T. brucei* and *T. vivax*, the last does not exist in Tinde. Schilling found it only once in the blood of a calf which had been infected by flies brought from Masumbwe, 77 miles away. In view of the scarcity of the spontaneous infection, and of the difficulty in getting sufficient quantities of the parasite, it was considered unnecessary to immunize against *T. vivax*. This, Schilling says, proved to be "a bad mistake."

When the inoculations and vaccinations were completed, the calves (and their mothers) were sent from Tinde to Masumbwe on June 25, 1934. This small village was chosen because previous attempts to keep cattle there had always ended in their destruction by nagana. Schilling had to leave Masumbwe in November, but the calves were left under the observation of a native Veterinary Assistant and under the control of HORNBY. Schilling has received notes on the behaviour of the animals up to January 31, 1935.

The first series was premunized by the minimal infection method, not more than 50 parasites being given in one dose. If trypanosomes did not appear in the blood of the inoculated animal within about a fortnight, and if the calf showed no signs of sickness and had increased in weight, the injection was repeated. Of the 23 calves treated in this way, 13 (57 per cent.) were alive after 7 months in tsetse areas, but for various reasons these figures required modification. For one reason or another Schilling eliminates 11 of the 23 animals and states that of the remaining 12 only one (9 per cent.) has died.

In the second group, a vaccine was used as antigen. Rats infected with *T. brucei* or *T. congolense* were killed when their blood was swarming with trypanosomes. The blood was defibrinated and dried in a shallow dish by fanning. Unfortunately, it was not found possible to keep the material sterile, so that after subcutaneous injection of the dark-brown emulsion (1 : 10 of sterile water) suppuration occurred in many cases. As a rule, 10 to 20 cc. of the above emulsion were injected. Of two calves which had been given one injection of vaccine only and had been bitten by infected flies 22 days later, one died 15 weeks and the other 36 weeks afterwards. Ten calves had 4 injections of vaccine at fortnightly intervals. Seven months later 9 were still alive.

A third group of five calves was exposed to infected flies, and when trypanosomes were found in the blood the calves were given half the curative dose of antimosan in two injections; 4 of the 5 animals are dead.

Of the 13 control calves, 8 (61 per cent.) are dead, and of the 31 cows not premunized 16 (51 per cent.) died within 7 months and all the rest were infected.

Schilling says that the number of his experiments is small, but the results obtained, viz. : 70 to 91 per cent. of the premunized animals alive, and only 39 per cent. of the non-premunized calves, suggest that there can be no doubt that the difference is a really significant one. He considers that the experiments should be continued and lays down certain rules for the guidance of those who may work on the subject in the future. It is emphasized that only calves which are thriving well should be used and that premunition must be performed against all three species of trypanosomes ; the rare *T. vivax* must not be neglected, as it sometimes produces quite deadly infections in cattle. At the present time it cannot be said definitely which of the two methods of premunition gives the better results. In favour of the minimal infection method is the simplicity of the technique ; this method is nearest to Nature's process, but a loss of 26 per cent. from the inoculation as was obtained in the present experiments is too high. Schilling believes that it can be lowered by more exact counting of the number of parasites injected. A very important matter is the proper choice of the season for the experiments, the time of reaction must coincide with the season of richest food supply, that is during the beginning of the rains.

A few experiments on pregnant cows indicate that there is a possibility that we can imitate the natural process of immunization of game still more closely by influencing the foetus *in utero* by a labile infection produced in the organism of the mother cow. W. Y.

KLIGLER (I. J.) & COMAROFF (R.). **Susceptibility and Resistance to a Trypanosome Infection. IX.—Active Immunization of Rats and Guinea-pigs and Passive Immunization of Rats to a Trypanosome Infection.**—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 145–160. [24 refs.]

The experiments described in this paper were devised with the object of studying the mechanism of resistance to trypanosome infections. On the one hand the authors attempted to ascertain whether immunity can be produced in rats, guineapigs and rabbits by repeated injections of dead trypanosomes ; and on the other hand they have studied the possibility of passive immunization of rats by the injection of the serum of guineapigs, rabbits and cats containing demonstrable trypanolytic antibodies.

Experiments are recorded in detail and the results summarized in tables. It was found that one or more injections of a suspension of dead trypanosomes (vaccine) increased the resistance of the rats to an infection with the same organism. The resistance produced by 20 injections was, however, not greater than that produced by 10 injections. Four rats out of more than 100 used in these experiments completely resisted infection ; 3 of these remained immune for a period of two months, after which they reacted in the same manner as the control animals. After repeated injections the blood of 2 of 10 rats tested contained demonstrable quantities of lytic antibodies.

The authors believe that the enhanced resistance in the rat produced by vaccination is due chiefly to an activation of the reticulo-endothelial system. They base this conclusion on the following observations :—
(1) Injection of dead trypanosome suspensions increased the resistance of treated rats ; (2) injection of dead trypanosome suspensions mobilize

the large mononuclear cells in the peritoneal cavity ; and (3) the loss of the enhanced resistance following splenectomy.

It was found that the intravenous injection of the specific vaccine into rabbits resulted in the production of a specific lytic antibody. Lytic serum taken from infected guineapigs and cats, after a crisis, when injected into rats, prior to, or shortly after, inoculation with trypanosomes resulted in a retardation of the infection.

The general conclusion drawn by the authors from this work is that in the rat the enhanced immunity resulting from the injection of dead trypanosomes is due to an activation of the reticulo-endothelial system.

W. Y.

RODHAIN (J.) & BRUTSAERT (P.). L'évolution des *Trypanosoma lewisi* et *Trypanosoma cruzi* chez *Melophagus ovinus*. [Development of *T. lewisi* and *T. cruzi* in *Melophagus ovinus*.]—C. R. Soc. Biol. 1935. Vol. 118. No. 12. pp. 1228-1231.

Experiments are described showing that *T. lewisi* and *T. cruzi* can develop in *Melophagus ovinus* with the appearance of metacyclic trypanosomes in the posterior part of the intestine.

The authors point out that the digenetic trypanosomes can be divided into two groups according to whether their development in the invertebrate host takes place in the anterior or posterior part of the intestine. The trypanosomes of the first group are inoculated by the bite of the infected insects (tsetse) and they are pathogenic to the vertebrate host. Those of the second group reach the vertebrate through the faeces of the invertebrate ; except for *T. cruzi* they are non-pathogenic, and they are also distinguished from the first group by the fact that they are readily cultured and by their perfect adaptation for the invertebrate host. In nature, as in the laboratory, a large proportion of the invertebrate hosts becomes infected, and furthermore many of them can be transmitted by a number of invertebrates. For example, *T. lewisi* can develop not only in *Ceratophyllus fasciatus*, the common rat flea, but also in *Xenopsylla cheopis* and in *Ctenopsylla musculi*, *Ct. canis*, and *Pulex irritans* ; and BRUMPT has shown that it can also develop in the flea of the swallow, *Ceratophyllus hirundinis*. *T. cruzi* on the other hand develops in many species of reduviid bugs, in *Cimex lectularius*, *C. rotundatus* and *C. boueti*, and also in certain ticks, e.g., *Ornithodoros moubata* and *Rhipicephalus sanguineus*.

A number of experiments were conducted to see whether these two trypanosomes would develop in *Melophagus ovinus*. The arthropods obtained from pupae were placed on guineapigs infected with *T. cruzi* or on rats infected with *T. lewisi* for two or three days and were then fed on clean animals. The lice passed part of each day on the experimental animal and were kept at night in tubes containing hairs of guineapigs or rats and fragments of blotting paper. It was found to be important to keep the temperature about 25°C. and the atmospheric humidity about 60°C. Even with these precautions the experiments could not be prolonged beyond 20 days.

Of 24 *Melophagus* fed on rats infected with *T. lewisi* 7 showed developmental forms in their mid-gut and 1 exhibited a permanent infection of the posterior gut. Of the 42 *Melophagus* fed on *T. cruzi* infected animals 8 showed cultural forms in the mid-intestine. Guineapigs and rats inoculated from the infected *Melophagus* became infected.

W. Y.

- i. MAZZA (Salvador). Investigaciones sobre la enfermedad de Chagas. I. Hallazgo de tripanosomas en murciélagos del Chaco y Ledesma, Jujuy. Presenta identidad de estos flagelados con *Schizotrypanum cruzi*, Chagas, 1909. [Studies in American Trypanosomiasis (Chagas's Disease). I. Discovery of Trypanosomes in Bats in Chaco and Ledesma, Jujuy.]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina Jujuy*. 1935. Publicación No. 22. pp. 1-11. With 6 figs. (1 coloured). [11 refs.]
- ii. — & MIYARA (J. S.). II. Sobre el hallazgo de un nuevo edentado, huesped natural de *Schizotrypanum cruzi* en la provincia de Mendoza. [II. Another Natural Host of *T. cruzi* in the Province of Mendoza.]—*Ibid.* pp. 11-16. With 3 figs. [12 refs.]
- iii. ROMAÑA (Cecilio). III. Acerca de un síntoma inicial de valor para el diagnóstico de forma aguda de la enfermedad de Chagas. La conjuntivitis esquizotripanósica unilateral (Hipótesis sobre puerta de entrada conjuntival de la enfermedad). [III. An Important Early Symptom of Chagas's Disease.]—*Ibid.* pp. 16-28. With 5 figs.
- iv. MAZZA (Salvador), MIYARA (S.), BASSO (G.) & BASSO (R.). IV. Comprobación de *Triatoma platensis* Neiva 1913 en la provincia de Mendoza. [IV. *Triatoma platensis* Neiva in Mendoza Province.]—*Ibid.* pp. 29-30.

A series of papers adding to our knowledge of Chagas' disease, its natural hosts and its vectors.

i. The author records the finding, for the first time in the áreas concerned, Resistencia, Chaco, and Ledesma, Jujuy, of certain trypanosomes in bats of the species *Nyctinomus macrotis*. In both the places mentioned the local *Triatoma* have been found heavily infected with evolution forms of *T. cruzi*. "Some time ago" a human case of Chagas' disease was observed in Ledesma and according to the author, though the record has not yet been published, two of his pupils have just confirmed the existence of cases in Resistencia. He is of opinion that the forms found in the bats are also *T. cruzi*.

ii. That the armadillos, *Dasyus unicinctus*, *D. sexcinctus*, *D. novemcinctus* and *Chaetophractus vellerosus* are natural Brazilian hosts of *T. cruzi* has been known for some time. The parasite has now been found also in another armadillo, *Zoëdyus pichy caurinus*, captured in San Carlos, Province of Mendoza. The trypanosome was seen in blood smears. Histological examination of the organs proved negative, but inoculation of the blood into white mice resulted in a month in the appearance of *T. cruzi* in the circulation, and a second inoculated with the citrated blood of this also showed infection after a similar interval.

iii. Nine cases of Chagas' disease in children between 1 and 10 years of age are recorded. In all but one a very early symptom was oedema of an eyelid with no pain but with conjunctivitis. The parents usually ascribed it to the bite of an insect, a bug (vinchuca), and there is an associated adenitis, pre-auricular, parotid or submaxillary. The swelling may be very marked, so that the eye cannot be opened. Further examination may reveal rise of temperature, increased pulse-rate, enlargement of liver and spleen. The oedema may spread widely.

Experimentally, conjunctival inoculation may result in setting up the disease and the author suggests that this is the usual portal of entry, seeing that this conjunctivitis and local oedema is so frequently an initial symptom. [Observation of a larger series of cases would serve to show whether this ocular lesion occurs more frequently than would be explained by the bug biting the closed eyelids or near them and the child inoculating the wound by rubbing.]

iv. Examination of bloodsucking Hemiptera in the Province of Mendoza has shown that, besides *Triatoma infestans*, another species *T. platensis* is found. It was first reported in 1913 in the Santa Rosa department of this Province. More recently it has been encountered in other departments also, Las Heras, Lavalle and Guaymallén, in the compounds where goats are kept and in human dwellings; in the latter *T. platensis* was present together with *T. infestans* infected with metacyclic forms of *T. cruzi*. [It is not clear in the article whether this infection applied to both species or to *T. infestans* only.]

H. H. S.

MALAMOS (B.). Ueber Vorkommen von *Schizotrypanum cruzi* bei Affen in Niederländisch-Indien. [The Occurrence of *T. cruzi* in Monkeys from Dutch East Indies.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Apr. Vol. 39. No. 4. pp. 156–171. With 16 figs. [23 refs.]

This paper records the discovery of *T. cruzi* in a number of *Cynomolgus* from Java.

After pointing out that hitherto *T. cruzi* has not been found in man or animals outside the American continent, the author states that whilst examining for malaria parasites a group of 10 young *Macacus cynomolgus*, which had recently arrived in Hamburg from Java, trypanosomes were found in two of them. A third was also proved to be infected through subinoculation of its blood into other monkeys. The remaining monkeys were examined for latent infection by means of the xenodiagnostic test of BRUMPT, and still another was found to be infected.

None of the infected animals exhibited any signs of disease. The findings in the peripheral blood varied; sometimes scanty trypanosomes could be found for a number of days, and at other times the blood was negative. A detailed account is given of the morphology of the parasite and of its pathogenicity for other monkeys and various laboratory animals. *Triatoma infestans* were readily infected and the faeces of the infected bugs produced subacute infections in mice. Study of the pathological anatomy of infected monkeys revealed the usual foci of leishmania forms in the heart and skeletal muscles, and in the lungs, liver, kidney, spleen, lymph glands and suprarenals. In fact all the findings indicate that the parasite in question is identical with *T. cruzi*.

W. Y.

REICHENOW (Eduard). Beiträge zur Kenntnis der Chagaskrankheit. [Contribution to Knowledge of Chagas' Disease.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. Nov. & Dec. Vol. 38. Nos. 11 & 12. pp. 459–477; 499–518. With 6 figs. [38 refs.]

In 1932 the author went to Guatemala to investigate the conditions of the workers on the plantations of Ludwig Nottebohm, especially in respect of malaria and hookworm. He soon found that Chagas' disease provided a good field for investigation, and the present paper describes the result of his work in this direction.

The author first worked in the neighbourhood of Las Viñas, which lies about 40 km. south of the capital of Guatemala. He found that the primitive dwellings of the plantation labourers were heavily infested with *Triatoma dimidiata*. Over the greater part of Guatemala the primitive rural houses are built of mud, and when the mud dries

deep fissures are formed which are ideal hiding places for the bugs. As the insects cannot be got at in these shelters the older huts are infested to an astonishing degree. Details are given regarding the habits of the *Triatoma* and their geographical distribution in Guatemala. They seem to occur everywhere, except in certain places in the west of the country near the Mexican frontier.

Wherever *Triatoma* were captured a certain number were found to harbour flagellates in their intestine. Apparently 29 to 35 per cent. of the insects were infected with a flagellate which animal inoculations showed to be *T. cruzi*. It was established that the infection spread chiefly directly from insect to insect through coprophagy. In 39 per cent. of the bugs a gregarine was found which could only be spread in this manner. It is presumably upon the frequency, or the reverse, of passage through the vertebrate host that the differences in virulence exhibited by various strains of *T. cruzi* depends.

Turning to the question of natural infections of vertebrates, the author writes that the chief sources of blood in the huts, apart from men, are dogs. Accordingly, the blood of numerous dogs was examined and in Las Viñas of 94 dogs 3 were found to be infected with *T. cruzi*; all the infected animals were about 2 months old, and as the 94 dogs included 12 of this age it appears that 25 per cent. of young dogs are infected. Among the older dogs only microfilariae were found on five occasions. Two armadillos and 14 bats were negative, and the trypanosome found naturally in monkeys belongs to a different species. The dog apparently is therefore the chief vertebrate host of *T. cruzi*. A large number of observations were made on the pathogenicity of Guatemala strains of *T. cruzi* for various laboratory animals and the results were compared with those given by a Brazilian strain; guinea-pigs, rabbits, mice, rats and dogs were used in this work. It was found that only in mice was the Guatemala strain moderately pathogenic; the Brazilian strain was much more pathogenic both for mice and young dogs.

The author next proceeded to make an exhaustive search for cases of human infection among children and adolescents. In the plantation village of Las Viñas the blood of about 100 young children was examined on three occasions and 3 were found to be infected. The infected children exhibited practically no symptoms and they remained free from signs of disease during an observation period of at least $1\frac{1}{2}$ years. Notwithstanding this considerable infection rate (3 per cent.) among the children no instance of chronic Chagas' disease was found among the inhabitants of Las Viñas.

The last portion of the work deals with the distribution and significance of Chagas' disease. Las Viñas constitutes the most northerly point in the known distribution of the disease. Although the disease has been known for 25 years the number of cases discovered has been small. In view of this the author has collected together all the recorded cases in which a definite diagnosis (parasitic) has been made and has recorded the place where they were discovered on a map of South and Central America. In this map he has also indicated the distribution of *Triatoma*. As the result of his analysis Reichenow believes that the infection in man, notwithstanding the small number of cases yet recorded, must be extremely common in South and Central America. The course of the acute infection differs according to differences in virulence of the trypanosome strain in the various countries; as a rule, it is favourable and only exceptionally, as in the Brazilian

state of Minas Geraes, is it threatening. It would seem as if the infection, after the acute stage is over, recovers spontaneously, and that there is no real evidence of a chronic stage of Chagas' disease.

W. Y.

VILLEGAS (Conrado). Dos nuevas observaciones de *Trypanosoma cruzi* en la Provincia de Córdoba. [Fresh Cases of *Trypanosoma cruzi* Infection in the Province of Córdoba.]—*Folia Biol.* Buenos Aires. 1934. Sept.-Oct.-Nov.-Dec. Nos. 42-43-44-45. pp. 200-201.

Many observers have remarked on the absence of symptoms in the Argentine in spite of infection with *T. cruzi*. The same held good in the two cases here recorded; the trypanosomes were found by chance.

The author was sent by the Director of the Institute of Hygiene, Cordoba, to determine the blood and splenic indexes in the Departments of Cruz del Eje and Minas which were believed to be endemic foci of malaria. He examined the blood of 200 persons by the thick drop method and among them found *T. cruzi* in two, a woman of 23 years and a girl of three. In the former only a single trypanosome was seen in the preparation, in the latter a score or so; both lived in Pichanas, Department of Cruz del Eje. Both persons appeared to be in perfect health. Inoculation of 1 cc. of the child's blood into the peritoneal cavity of a young white rat resulted twelve days later in the presence of trypanosomes in small numbers in the peripheral blood.

H. H. S.

ROMAÑA (Cecilio). Tripanosomiasis americana y bocio endémico. Estado actual de la cuestión. [American Trypanosomiasis and Goitre.]—*Semana Méd.* 1935. Mar. 21. Vol. 42. No. 12 (2149). pp. 897-902. [13 refs.]

This article summarizes the present state of the question as to whether there is any aetiological connexion between Chagas' disease and enlargement of the thyroid.

The author gives a quotation from CHAGAS' description of the disease which led him to conclude that the goitre was of trypanosomal origin. He next enumerates the arguments in favour of the theory, with brief comments on each: (1) That the condition of myxoedema is often found in the acute cases and in the later chronic stages trypanosomes are present and the thyroid is enlarged. (2) That thyroid enlargement is common in regions where the disease was first studied, the northern Minas Geraes, and where other forms of the disease exist. (3) That the infectious theory of goitre has been widely accepted by those who have specially studied the condition and that "the goitre found in regions where Chagas' disease prevails is caused by the latter" [this would savour of a *petitio principii*]. (4) That intrauterine infection by trypanosomes would account for the congenital goitre observed in children inhabiting districts where Chagas' disease prevailed.

Of arguments against, the author gives the following: (1) That the myxoedema spoken of is found in human beings and even in animals who show no trypanosome infection. (2) That there are regions in Brazil and in the Argentine where the two diseases coexist, or are superposed and others where goitre has been known for a long time but where Chagas' disease is not met with. (3) The opposite

of the last, viz., that there are areas where the trypanosomiasis, both in acute and chronic stages, is present, but goitre is not observed. (4) That the pathology of the goitres associated with the trypanosome infection has not been closely studied in these districts till recently except in cases of chronic Chagas' disease, but now nothing characteristic has been found different from what is seen in endemic goitre in other parts of the world. (5) That in spite of all the experimental research carried out on this form of trypanosomiasis no investigator has recorded any predilection on the part of the parasite for affecting the thyroid gland, nor have they noticed hypertrophy of the gland as a result of their experiments. [The author does not include KRAUS's paper among his references. KRAUS, after some years' investigation, was very doubtful of any aetiological connexion between Chagas' disease and goitre (see this *Bulletin*, 1926, v. 23, p. 912).]

H. H. S.

FITTE (Oscar E.). Primer caso de tripanosomosis humana en la Prov. de La Rioja. [**First Case of Human Trypanosomiasis in La Rioja.**—*Prensa Méd. Argentina*. 1935. Feb. 27. Vol. 22. No. 9. pp. 432-433.]

The author has for some time been on the look out for cases of infection with *T. cruzi*, and when examining blood for malaria by the thick drop method has searched also for trypanosomes. He found them, though they were scarce, in the blood of a boy of 13 years showing no symptoms except some glandular enlargement. Their presence was confirmed by inoculation of 10 white mice each with 0.5 cc. of the patient's blood; one died four days later, the other nine gave positive results. The case is put on record as it is said to be the first reported from the Province of La Rioja in the Argentine.

H. H. S.

CHAGAS (Evandro). Infection expérimentale par le *Schizotrypanum cruzi* chez l'homme. [**Experimental Infection by *S. cruzi* in Man.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 7. p. 718.]

An experiment performed on a human being with the object of ascertaining whether *T. cruzi* is transmitted through the bites of infected reduviid bugs was negative.

Three larvae and one adult *Triatoma megista*, the faeces of which contained numerous crithidia and metacyclic forms of *T. cruzi*, were allowed to feed on the forearm of the patient, care being taken that no faeces were deposited on the skin during the meal. The patient, who was carefully observed for a period of 30 days, failed to show any signs of infection. As previous observations had shown that the incubation period of this infection in man is only 10 to 12 days, Chagas concludes from the present experiment that *T. cruzi* is not transmitted to man by the bite of *Triatoma*.

W. Y.

BONACCI (Humberto). Nuevo medio de cultivo para el *Trypanosoma cruzi* Chagas, 1909. [**A New Medium for cultivating *T. cruzi*.**—*Rev. Inst. Bacteriológ.* Buenos Aires. 1934. Mar. Vol. 6. No. 2. pp. 242-247.]

The author gives three formulae, of nutrient agar differing very slightly. He calls them Nos. 1, 4 and 9. No. 1 is a nutrient broth with Witte's peptone 1.5, NaCl 0.5 and agar 1 per cent. No. 4 has

2.5 per cent. peptone and 0.7 per cent. NaCl, and No. 9 3 of peptone and 0.7 NaCl. The mixture is made neutral to litmus, heated to 115°C. for 20 minutes, filtered through cotton wool and placed in Erlenmeyer flasks, 100 cc. in each and sterilized in the autoclave at 110°C. for 20 minutes. This nutrient agar forms the basis of his medium to prepare which the agar is melted, cooled to 50°C. and to it are added 0.5 per cent. glucose and 5 per cent. sterile whole blood of a young guineapig and the medium distributed in test-tubes. The optimum temperature for cultivation is 25°C.

The author has successfully inoculated animals with such a culture and symptoms appeared after 10 days' incubation and the trypanosomes persisted in the peripheral blood for 39 days. The most sensitive animals for the experiments were puppies and next in order white rats, kittens and guineapigs. Noguchi's medium, he states, is not so good for isolation of the trypanosome, but is excellent for preserving the strains and has the further advantage of being able to adapt itself to temperatures above 25°C. The author claims that his medium is very useful for early diagnosis of suspected cases. H. H. S.

DIAS (Emmanuel). [In Portuguese & French.] *Trypanosoma cruzi* ou *Schizotrypanum cruzi*? [Is *T. cruzi* or *S. cruzi* **Correct Nomenclature**?]—*Mem. Inst. Oswaldo Cruz*. 1934. Vol. 29. No. 1. In Portuguese pp. 203–215. With 1 fig. [42 refs.] In French pp. 217–227. With 1 fig.

This paper is devoted to a discussion of the systematic position of the parasite of Chagas' disease, known under the names *Trypanosoma cruzi* and *Schizotrypanum cruzi*, each of which has the support of authoritative writers whose opinions are critically examined by Dias.

The author himself maintains that the characters distinguishing this form from other trypanosomes provide sufficient grounds for recognizing it as a separate genus, under the name *Schizotrypanum cruzi*. These are (1) its intracellular situation in the tissues of the vertebrate host during multiplication, and (2) reproduction only in the leishmanial stage. The author, moreover, holds that *Schizotrypanum* is related to *Leishmania*, occupying an intermediate position between this genus and *Trypanosoma*. The latter genus is reserved for flagellates which multiply in the blood in the trypanosome stage. [It should be noted, however, that strictly speaking, the site in which a parasite develops is of no taxonomic value, the classification of animals being based on their morphological characters exclusively. The morphology of *T. cruzi* conforms to that of all trypanosomes, from which it differs only in its multiplicative phase. Since the stage in which reproduction occurs varies considerably in other trypanosomes, it cannot serve to separate *T. cruzi* from them generically. If this were done a number of other equivalent genera would have to be created. In view of these facts, it is advisable to retain CHAGAS' original name, *Trypanosoma cruzi*.] C. A. Hoare.

ZUMPT (F.). Zur Systematik der *Glossina palpalis*-Gruppe. [The **Systematics of the *Glossina palpalis* Group**.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Apr. Vol. 39. No. 4. pp. 141–156. With 10 figs.

Transgressing the limits of his subject as indicated in the title, the author first considers subdivisions of the genus *Glossina*, and, relying

on characters afforded by the genital armature in both sexes, raises the *fusca*, *palpalis* and *morsitans* Groups of NEWSTEAD to subgeneric rank, employing respectively for the three subgenera so constituted the names *Austenina* (sunk more than a decade ago by NEWSTEAD), *Nemorhina*, and *Glossina* (*sensu stricto*). A table is then given for the distinction of the species included under the subgenus *Nemorhina* (i.e., the *G. palpalis* Group), among which are *G. fuscipes*—generally regarded, even by its author, as a subspecies of *G. palpalis*, but restored by Zumpt to specific rank—and what is described as *G. martinii*, sp. nov. The latter, the typical material of which was taken in Tanganyika Territory (at Bismarckburg, near the extreme southern end of L. Tanganyika), though indistinguishable from *G. palpalis* and *G. fuscipes* by means of external characters, exhibits certain differences, considered by the author to be of specific value, in the shape of the inferior claspers.

[Whether, in the absence of all other characters, slight differences in the inferior claspers are really of specific value is a matter which must be left to the individual opinions of experienced systematists. The present reviewer, at any rate, is inclined to think that, pending the crucial test of mating, it will be well to continue to regard *G. fuscipes* as a form of *G. palpalis*, and to treat *G. martinii* likewise.

The use by the author of the terms outer and inner *parameres* (borrowed from mosquito terminology, in which they are applied to parts of the penis) for the superior and inferior claspers is to be deprecated.]

E. E. Austen.

NASH (T. A. M.). **The Identification of the Three Commonest Species of Nigerian Tsetse Fly.**—3 pp. With 5 diagrams. 1934. Aug. Printed by Survey Department, Lagos.

This is a useful two-page leaflet describing and illustrating by line blocks certain differences between *Glossina palpalis*, *tachinoides* and *morsitans*. It is intended for the use of those who have no knowledge of entomology. Clearly such leaflets as these might be of considerable value in many parts of Tropical Africa.

P. A. Buxton.

NASH (T. A. M.). **The Effect of High Maximum Temperatures upon the Longevity of *Glossina submorsitans*, Newst., and *G. tachinoides*, Westw.**—*Bull. Entom. Res.* 1935. Mar. Vol. 26. Pt. 1. pp. 103–113. With 2 figs.

In the north of Nigeria the climate is extremely hot and dry in March and April. What is the effect of this on adult *Glossina*, exposed in cages to conditions prevailing in the shade?

At the beginning of each month groups of freshly emerged fly (*G. submorsitans* and *tachinoides*) were put in small cages, and exposed to shade temperature in a hut with a good thatch roof but no sides: the conditions are approximately those which prevail in a dense thicket. The flies were offered an opportunity of feeding daily. Experiments were carried out in the four months January to April, the temperature rising steadily throughout this period. The mean length of life fell from about 25 days in January to about 3 in April. Moreover, a consideration of the number of deaths and of the maximum temperature on individual days shows clearly that temperatures above 100°F. (37.8°C.), and particularly above 103°F. (39.4°C.) are followed by a high mortality. It seems that *G. tachinoides* are killed by rather lower temperatures and shorter exposures than are *submorsitans*.

It is encouraging to observe that these figures, obtained under semi-natural conditions, agree in essentials with those which BUXTON and LEWIS obtained under strictly defined laboratory conditions [*ante*, p. 369]. It seems highly probable that the high temperature in the region where these experiments were carried out, causes a high mortality in nature at this season of the year. If this is so, then as the author suggests, a very restricted thinning of trees in the permanent breeding places might result in local extermination of the fly.

P. A. B.

MERKEN (G.). Pièges Harris. [**Harris Traps.**].—*Bull. Méd. du Katanga*. 1934. Vol. 11. No. 5. pp. 154–157.

It appears that the Belgian as well as the Congolese daily papers have been booming the Harris traps as capable of clearing the Belgian Congo of sleeping sickness. The author points out that ideal conditions for the traps are rarely to be found in the haunts of *G. palpalis*. These haunts are in deep, heavily shaded forest galleries, sunless for most of the day and it is not practicable to make clearings for the traps. In any case the traps will not catch all the tsetses.

A. G. B.

JACONO (Igino). Osservazioni sui tripanosomi e proposta di una nuova classifica. [**A New Classification of Trypanosomes.**].—*Ann. di Med. Nav. e Colon.* 1935. Jan.–Feb. 41st Year. Vol. 1. No. 1–2. pp. 1–18. With 20 figs.

Having studied the somewhat striking trypanosomes which occur in frogs the author attempts a new classification of the group into two genera, the one (*Trypanosoma*) to include those of the type he has studied and the other (*Castellanella*) all other trypanosomes. There would seem to be little justification for this procedure which appears to the reviewer to be quite artificial.

C. M. Wenyon.

GRALL (G.). L'action thérapeutique du service de la trypanosomiase en A.O.F. jugée par les Bandas de l'Oubangui-Chari: le "ballet de la maladie du sommeil."—*Ann. de Méd. et de Pharm. Colon.* 1935. Jan.–Feb.–Mar. Vol. 33. No. 1. pp. 144–146.

SCHILLING (Claus). Die Bekämpfung der Tsetsefliege im früheren Deutsch-Ostafrika.—*Deut. Med. Woch.* 1935. Mar. 15. Vol. 61. No. 11. pp. 427–428.

MALARIA.

WATSON (Malcolm). *Some Pages from the History of the Prevention of Malaria.*—*Glasgow Med. Jl.* 1935. Feb., Mar. & Apr. Vol. 5. Nos. 2, 3 & 4. pp. 49-70; 130-153; 202-220. [79 refs.]

Sir Malcolm Watson commenced his lecture with a sketch of the work in Malaya, begun in 1901, and described by Ross as the first successful anti-malarial work in the British Empire. He drew particular attention to the decrease in deaths from other diseases which followed the successful control of malaria. He stated that an important factor which contributed to his success was the combination of clinical observations made in the hospital with epidemiological observations made in the field; he was himself physician, health officer and entomologist, there was perfect co-operation with the engineer. "I want to emphasize," he said, "that our success has come from the knowledge acquired not in the hospital alone, nor in the laboratory alone, but by co-ordinated work in all three, and it led to discoveries in clinical medicine, protozoology, ecology and epidemiology of fundamental importance in the prevention of disease."

While he was a busy practitioner and the sole European medical officer in a coast district a hundred miles long, Watson yet managed to make discoveries of inestimable value. "In my little laboratory I was breeding mosquitoes, discovering new species of mosquitoes, recognizing structures that enabled me to construct a key for the identification of the larvae of certain species of anopheles, a matter of great practical importance. In the field I was studying the biology of the insects. . . . As medical officer, I saw and treated the sick in hospital."

As a striking example of what can be accomplished by mosquito control, he retold in his lectures the story of Carey Island where control has been in force from the opening of the rubber estate in 1906. Carey Island is really a fresh-water swamp on clay soil, surrounded by salt water; conditions which are notorious for producing the most appalling malaria. It has always remained healthy, and Sir Malcolm quotes his successor Dr. Barclay BARROWMAN who wrote in 1934, "On Carey Island, with a population of over 5,000 . . . there has been one child with enlarged spleen during the past five years, and she had arrived on the estate with the spleen already enlarged. The infection rate among the total population for the past five years has been under one-tenth per cent. per annum. . . . there is rapidly growing up a locally-born labour force—18 per cent. of the present population was born on the estate. There are over 1,500 healthy happy children, among whom the sick day rate last year was no more than 0.4 per cent."

After Watson had dealt successfully with the malaria of the coast and flat land, due to *A. ludlowi* and *A. umbrosus*, he was faced with the problem of malaria of the inland hills and ravines, carried by the stream-breeder, *A. maculatus*. "What the country required was some new method of preventing the disease. To this I now turned my attention . . . I had a deep conviction that this deadly *A. maculatus* could be exterminated if appropriate measures were adopted. So I devised a system of subsoil drainage of valleys. . . . The system proved a success . . . We still required a quicker and less expensive method of controlling malaria than subsoil drainage. This was provided by my discovery in 1914 of a mixture of mineral oils which

completely destroyed *A. maculatus* when applied once a week to fast-running streams. . . . The value of this discovery was quickly appreciated, and the use of this anti-malarial mixture spread throughout the peninsula, with the happiest result . . . most unfortunately, I did not publish this discovery until 1921. Had I done so, the story of malaria in many parts of Macedonia during the Great War might have been very different." After relating the success attained by his method, in the rubber estates of which he was in medical charge, the lecturer spoke of the work begun in Singapore in 1911. "This city was next off the mark. . . . Within the municipality in 1932 there were 41.25 miles of concrete channels, 72.63 miles of subsoil pipes, and over 300 miles of earth ditches; 18,682 gallons of anti-malarial mixture were used. . . . In the Federated Malay States the Government next took up the work, and in November 1911, the Malaria Advisory Board began work. . . . For the year 1926 . . . the expenditure on malaria by the F.M.S. Government was £104,400."

In speaking of prevention by treatment, the lecturer said, "There is, in my opinion, no antagonism and no competition between the various methods of preventing malaria. . . . In all campaigns anti-malarial drugs have a place." He spoke of the work of GORGAS in Havana and in Panama in terms of highest praise. "It had been proved that both malaria and yellow fever were carried by mosquitoes; and it had already been proved in Havana (1901) Klang (1901) and Ismailia (1902) that these diseases could be brought under control, or for all practical purposes abolished, when the mosquitoes carrying them were reduced below a certain number."

W. Fletcher.

- DE LANGEN (C. D.) & STORM (C. J.). **Observations on the Modern Medical Treatment of Malaria. A Clinical and Experimental Study.**—*Far Eastern Assoc. Trop. Med. Trans. Nank. Congress, Nanking, China, 1934* Vol 2 pp. 233-260. With 16 figs. on 12 plates.
- HOOPS (A. L.). **Observations on the Prophylaxis and Cure of Malaria with Atebrin on Malacca Rubber Estates during Two Years (July 1932 to June 1934); with a Note on the Prevalence of Malaria on these Estates since 1925.**—*Ibid.* pp. 261-280 [32 refs.]
- YAO (Y. T.) & JUNG SUN (C.). **Field Experiment on Malaria Treatment. A Comparative Study of the Therapeutic Value of the Various Anti-Malaria Remedies.**—*Ibid.* pp. 281-297. With 2 charts. [15 refs.]
- WALCH (E. W.) & SOESILO (R.). **Malaria Control in the Netherlands Indies.**—*Ibid.* pp. 191-200. With 15 figs. (13, 1 coloured, on 7 plates).
- SCHARFF (J. W.). **Anti-Mosquito Measures in the Northern Settlement of Malaya.**—*Ibid.* pp. 201-212. With 5 plates & 3 figs.
- YAO (Y. T.) & WU (C. C.). **Antilarval Measures by the Use of Paris Green in a Selected Area of Nanking.**—*Ibid.* pp. 213-221. With 3 charts.
- RUSSELL (Paul F.). **The Automatic Distribution of Paris Green for Control of Anopheles Larvae.**—*Ibid.* pp. 223-232. With 2 text figs. & 3 figs. on 2 plates.
- YAO (Y. T.) & WU (C. C.). **One Year's Observation of *A. hyrcanus* var. *sinensis* in Nanking, 1933.**—*Ibid.* pp. 3-26. With 3 maps. 2 graphs & 2 figs. [12 refs.]
- & LING (L. C.). **Epidemiological Study of Malaria in Nanking.**—*Ibid.* pp. 89-106. With 3 charts. [18 refs.]
- JACKSON (R. B.). **The Anophelines of the Colony of Hong Kong. Some Observations on their Species, their Habits, and on the Results obtained from Dissections of Catches made on the Island and Mainland.**—*Ibid.* pp. 27-36.

TOUMANOFF (C.). Etude de l'indice maxillaire de Roubaud en tant que méthode pratique d'investigation sur les aptitudes trophiques des espèces anophélinennes d'extrême-Orient. [Roubaud's Maxillary Index as a Practical Method of Investigation of the Trophic Aptitudes of Anopheles.]—*Ibid.* pp. 37-51. With 9 figs. & 3 charts.

WALCH (E. W.) & WALCH-SORGDRAGER (G. B.). The Eggs of Some Netherlands-Indian Anophellines.—*Ibid.* pp. 65-81.

MORIN (Henry G. S.), BADER (H.), MONNIER (E.) & MOREAU (P.). Recherches sur la concentration en chlore du sang chez les paludéens au Tonkin. [The Blood Chlorine in Malarials at Tonking.]—*Ibid.* pp. 165-190. With 7 graphs. [49 refs.]

WILLIAMSON (K. B.). Need for Action in Relation to the Biochemical Investigation of Anopheline Breeding Places.—*Ibid.* pp. 83-87.

Many valuable papers were contributed to the section on malaria at the Nanking Meeting of the Far Eastern Association of Tropical Medicine. Of special note was a defence of quinine against the newer remedies by Professor de LANGEN: an account of malaria control in the Dutch Indies by the late Professor WALCH; malaria control in Penang by Dr. SCHARFF; *A. maculatus* in Hong Kong by Dr. JACKSON; the maxillary index in the anopheles of Indo-China by Dr. TOUMANOFF.

Professor C. D. DE LANGEN and Dr. C. J. STORM presented an account of a clinical and experimental study of the action of quinine, plasmoquine and atebtrin upon the organs of the body. They argue that these drugs do not act directly on the parasites but probably indirectly by stimulating the natural defence reactions of the organism, and that therefore the question of the general action of these remedies on the organism is of great importance. As the indirect route of action is the most probable one, figures intended to prove the superiority of one remedy over another in the matter of destroying the parasites are completely worthless. "The results in London, Hamburg, Amsterdam and other places in Europe with individual treatment must in no way be regarded as giving guidance for treatment in the real malaria countries."

The three remedies differ in their action on the liver. (a) Quinine does not damage it, and even in undernourished persons it will not produce urobilinuria. (b) Atebrin produces no urobilinuria in healthy people, but urobilin appears if there is malnutrition and the liver is poor in glycogen. (c) In fatalities due to plasmoquine the liver is always damaged. "Quinine exerts a favourable action on the functions of many organs. . . This is of great importance for the treatment of malaria patients. In criticising other products offered as remedies for this disease, it is therefore not sufficient that we should ask ourselves if they are toxic for the various organs, but also if they possess the same good general properties possessed by quinine. Such properties are not yet known in the case of plasmoquine and atebtrin."

The authors have carried out a series of experiments with *Macaca irus* (*Cynomolgus*) in investigating cardiovascular disturbances following injections of the three drugs. Several reports have already been published on the circulatory disturbances which may follow the therapeutic administration of atebtrin. When atebtrin or plasmoquine was perfused through the isolated heart of a monkey, the rhythm of the organ became irregular, then it stopped and perfusion with pure Tyrode's solution did not start it again. Quinine did not produce irregularity of the contractions, and when the heart was stopped by very strong solutions of the drug it could be started again by perfusion

with pure Tyrode's solution. The total quantity of fluid flowing through the coronary vessels per minute diminished after the addition of either plasmoquine or atebtrin, but after the addition of quinine it increased. The vasoconstriction which follows plasmoquine and atebtrin throws a strain upon the heart. "While the fall in blood pressure following quinine must certainly be attributed to a vascular dilatation, that caused by plasmoquine and atebtrin appears principally due to damage of the heart's action." When the vasomotor centre is intact, stimulation of a sensory nerve is followed by a rise of blood pressure. This reflex is not abolished by quinine. "That the reflex disappears after plasmoquine and atebtrin must be attributed to a direct toxic action of these drugs on the vasomotor centre. . . both atebtrin and plasmoquine, but especially the latter, are more toxic for the heart and vascular system than is in general admitted. . . . Moreover, since the administration of these drugs by routes other than the mouth is becoming more and more fashionable, it may be expected that untoward side-effects on the part of the circulation and respiration will become more and more common. . . . Apart from the direct, injurious organotropic action [of plasmoquine and atebtrin] on the organs themselves, for instance the liver, it is also possible that in this way indirectly the development of that natural immunity on which recovery depends could be retarded." While quinine employed clinically restores extrasystolic arrhythmias to normal rhythm, atebtrin and plasmoquine produce such irregularities themselves. It is therefore advisable that when atebtrin and plasmoquine are administered, quinine should be given with them because of its steadying effect upon the circulation.

This paper was followed by one in which Dr. A. L. Hoops gave an account of the great success of atebtrin as used on the rubber estates of Malacca (see this *Bulletin*, Vol. 31, p. 695). He concludes that: "Atebtrin is the best drug available for the treatment of all types of malaria in Malaya, especially in the case of controlled populations. . . . Atebtrin is greatly superior to quinine in the prevention of relapses; judging by present experience with atebtrin, relapse rates do not exceed 5 to 8 per cent. in subtertian, and 5 to 16 per cent. in benign tertian malaria. . . . On estates, the cheapest and best measures are to continue antimalarial work in the danger zones, and to treat cases of malaria with atebtrin. . . . A short course of plasmoquine, not exceeding 0.03 gram daily for from 5 to 8 days, should be given after atebtrin treatment in subtertian malaria." [See p. 418 above, and also HECHT and EICHHOLTZ in this number.]

Dr. G. T. YAO and Dr. C. JUNG SUN reported on the treatment of 281 cases of malaria with different drugs. The drugs employed were totaquina types I and II, atebtrin, quinoplasmoquine, and quinine. All of them were found equally effective in reducing the number of parasites, with the exception of crescents, in all three types of infections. Vomiting was the only toxic symptom; this occurred in 5.5 per cent. of the atebtrin treated cases and in a smaller proportion of those treated with the other drugs. Quinoplasmoquine was the most effective in reducing the size of the spleen.

Professor E. W. WALCH and Dr. R. SOESILO told the story of the successful struggle against malaria in the Netherlands Indies. Success has been won by antilarval control, and they write, "The value of *antilarval measures* for the control of malaria has been very much discussed in recent years and we therefore wish to emphasize that the improvements mentioned above have been obtained through antilarval

measures." Malaria prevails in its worst form in the coastal zone.

(1) The mangrove swamps are often free from malaria until they are interfered with, but, as soon as they are cleared, and the flow of water is hampered by footpaths, roads, and railway embankments, *A. ludlowi* var. *sundaica*, the most dreaded vector, and *A. subpictus* breed in the sunny, stagnant, brackish waterpools. (2) In other places, tides and currents lead to the silting up of the mouths of rivers; behind the sand bars, lagoons are formed, where floating algae develop in the brackish water and provide ideal breeding places for *A. ludlowi*. Sometimes this silting has been prevented by building piers to divert the sand, but the best way to deal with a river which does not carry enough water to keep its mouth open is to connect it with a more powerful stream by digging a canal parallel to the coast line. This method is not always possible, and filling, canalization, etc., have been employed. (3) The marine fishponds used to be responsible for very severe malaria. An edible fish called "Bandeng" is raised in these ponds, and formerly *A. ludlowi* bred freely among the floating algae on which the bandeng fed; the weeds protected the larvae from the small larva-destroying fish, *Panchax panchax*. These ponds have been dealt with by periodically draining them into the sea at intervals of about a month. This kills the floating algae and promotes the development of bottom algae which provide equally good nourishment for the bandeng. When the bottom algae float to the surface as the ponds refill, they form patches of compact scum. No larvae can breed in these patches, and the larvae in the open water between them are destroyed by their enemies the *Panchax*. (See *Bulletin*, Vol. 27, p. 640.) (4) The inland, fresh water fishponds, where "gorami" and "gold-fish" are raised for food are also responsible for much malaria which is carried in some places by fresh water *A. ludlowi*, and in others by *A. hyrcanus* var. *nigerrimus*. These inland ponds cannot be dealt with like those on the coast by opening sluice gates and letting them empty themselves into the sea. In some places, ponds situated on terraced hill sides have been drained, but elsewhere the economic loss entailed by destruction of the fishing industry could not be faced. Here again the mosquito larvae are sheltered by the aquatic vegetation; this is not used as a food by the fish—these feed on leaves and vegetables thrown into the ponds for the purpose. The fish-expert, REYNTJES, has discovered a fish, the so-called "Tawes" (*Puntius javanicus*) which feeds voraciously on the submerged vegetation, and soon causes it to disappear. Pictures are given showing first, a pond covered with weeds before the introduction of tawes, and secondly, the same pond later on after it had been cleared of vegetation by their agency. (5) Ricefields present another problem; generally speaking the wet ricefields are not dangerous, provided that they are supplied not only with efficient irrigation, but also with good drainage. The water on the coastal ricefields becomes brackish when irrigation is insufficient, and *A. ludlowi* breeds in them. Some of the valleys inland, lying at an altitude of about 1,000 feet, are watered by irrigation. At first, they were very fertile, and the natives exhausted the soil by too frequent planting; later, they became waterlogged and poor, because adequate provision for drainage had not been made. *A. aconitus* bred in the flooded fields; large areas were abandoned and formed pestilential swamps; the spleen rate was between 80 and 90 per cent. The measures adopted were attended with astounding success, they were: (a) A drainage system, (b) cleaning the grassy irrigation ditches

which bred *A. aconitus*, (c) the planting of rice only once a year, and that in the wet season, so that during the dry season the plain was dry and anopheles breeding impossible. As a result of this, the spleen rate of Tjirandjang which was 88 in 1918, was only 1 in 1931, while it was 98 in a neighbouring district where nothing had been done. (6) In the hilly and mountainous districts of the Netherlands Indies, the carriers are *A. maculatus* and *A. aconitus*, as in the Malay States, and the methods used there have been adopted.

Dr. J. W. SCHARFF, Senior Health Officer, Penang, described how 15½ square miles, embracing practically two-thirds of the population of rural Penang, had been "insured against the risk of malaria infection." The cost is heavy: a sum of \$50,000 (£5,833) was first made available for anti-mosquito work in 1924; this annual provision was repeated in 1925 and raised to \$75,000 (£8,750) in later years. The method adopted is to oil the breeding places of dangerous mosquitoes for a distance of half a mile from the outskirts of the village or area which is being dealt with; the proximal ravines are then drained and the oiling areas are extended further into the country, and are gradually linked up with other protected areas. A great deal of needless oiling is saved by reducing the area of the swamps and seepages in ravines. This is done by means of open drains dug along the edge, or contour, of the slope from which the water rises. Permanent anti-malaria drainage has been carried out in some populous areas; but, except under special circumstances, no scheme is undertaken unless permanent drainage can be completed for the price of 5 years oiling, or unless the whole of the anti-malaria work within the area can be carried out for under a dollar per head of the population served. Paris green has been found definitely less efficient and more costly than oil in the control of *A. maculatus*, the principal Malayan carrier. Earthen wells in which mosquitoes breed are treated with petrol once a week. Two ounces stirred in with a stick are sufficient for a well 4 feet in diameter, and after half an hour, no taste or smell remains. The wells used for irrigating gardens on the slopes of Penang Hill were formerly the source of much malaria. It has been found that when these are freed from aquatic vegetation, and filled by means of water splashing into them from a height of a few feet, no dangerous larvae can breed there. The effect of the measures adopted "has been to transform the appearance of villages. In place of miserable and weakly children there are now sturdy youngsters. Squalor that was induced by sickness has given way to comfort and good health."

Drs. Y. T. YAO and C. C. WU employed a 1 per cent. mixture of Paris green in road-dust as a larvicide in a selected area of Nanking with a population of 782, between August and December 1933. The incidence of both the adults and larvae of *A. hyrcanus* (the only anopheles) was greatly reduced. Dr. P. F. RUSSELL described an automatic distributor for Paris green, which is fixed over a stream and is worked by a paddle-wheel turned by the current. (See this *Bulletin*, Vol. 30, p. 864.) Drs. Y. T. YAO and C. C. WU gave the results of their observations on *A. hyrcanus* var. *sinensis* which is the only anopheles in Nanking. Out of 11,071 dissected, gut infections were found in 6. A number of laboratory-bred specimens were fed experimentally, with the result that some of them became infected with *P. vivax*. None of those fed on subtertian and quartan cases became infected. The authors found that *A. sinensis* would breed almost anywhere, but preferred water with plenty of vegetation, plenty of sunshine, still and clear, with a pH between

7.2 and 7.4. In a survey conducted by Dr. YAO and Dr. L. C. LING the spleen rate among the children was found to be 2.46. *P. vivax* accounted for 67 per cent. of all infections.

Dr. R. B. JACKSON presented a report on the anopheles of Hong Kong. He has made some interesting observations on the behaviour of *A. maculatus* in the colony. This mosquito is met with in hill streams throughout the year and constitutes the majority of the catch in these places. It is the most important carrier in Malaya, but in Hong Kong it is relatively harmless for it rarely comes into houses to bite man. This is not to be explained by the presence of large quantities of cattle, because there are few present. It is curious that, in Hong Kong, *A. maculatus* has been found in streams polluted by cow-byres, and in streams flowing through manured land. *A. minimus*, one of the two principal malaria carriers of Hong Kong, breeds in irrigation ditches and streams of flat grade amongst or near the hills. *A. jeyporiensis*, the other important carrier, breeds in abandoned terraced rice fields among the hills throughout the year, and in other rice fields when they are lai' fallow in the autumn. The range of flight of this mosquito much exceeds half a mile. *A. hyrcanus* breeds in stagnant water with vegetation. It is not an important carrier, but both this mosquito and *A. maculatus* can carry malaria under exceptional conditions such as are met with in large camps of labourers.

Dr. C. TOUMANOFF reported on the maxillary index of the anopheles of Indo-China. The results of his investigation support the theory of ROUBAUD, to the effect that this index is low in androphilous species. The author found that the index in the harmless, or relatively harmless, species differed distinctly from that of dangerous species, such as *A. minimus*. The maxillary index of *A. barbirostris*, *A. vagus* and *A. subpictus* was high, and it was found by means of precipitin tests, carried out in conjunction with Dr. J. MESNARD, that these mosquitoes fed on the blood of animals, while, on the contrary, 86.48 per cent. of the *A. minimus* examined were found to contain human blood. It was concluded that the maxillary index is a very valuable indication of the habits of an anopheline species.

Dr. E. W. WALCH and G. B. WALCH-SORGDRAGER contributed a paper on the eggs of some Netherlands-Indian anophelines. They observed marked differences between the eggs of *A. subpictus* in British India (where an infected specimen has never been found) and those of the Netherlands Indies (where it is sometimes a carrier).

Dr. Henry G. S. MORIN and his colleagues contributed a paper on the occurrence of corpuscular hyperchloraemia in malaria (this *Bulletin*, Vol. 31, p. 459) and Dr. L. A. ROBIN one on premunition among labourers working on estates (*loc. cit.*, Vol. 32, p. 142).

A paper was received from Professor J. B. WILLIAMSON urging that action should be taken with regard to the biochemical investigation of anopheline breeding places, and the Congress passed the following resolution:—

"The Ninth Congress of the Far Eastern Association of Tropical Medicine, recognizing the pressing need for co-operative investigations in the problems of malaria control wishes, in particular, to emphasize and direct attention to the fundamental importance in malarial epidemiology of studying bio-chemical changes occurring in the breeding places of anopheline mosquitoes.

"This Congress considers that advances of practical utility in the control of malaria might be made if the data obtained by workers in the countries of the Far East were made comparable.

"It is resolved, therefore, 'that, with the consent of the Governments concerned, such investigations, conducted in various countries, be co-ordinated through the appointment of a joint committee of chemists and malariologists resident in these countries.'

"It is recommended that this Committee should be invited to formulate the general lines upon which bio-chemical investigations shall proceed, and that they should be asked to report to the Director of the League of Nations Far Eastern Bureau concerning the principles and methods of study which are likely to be most profitable and from time to time concerning the results achieved from this application.

"The following experts shall be requested to serve as honorary members of this Committee.

"(1) Dr. R. Soesilo, Chief of Malaria Survey of Netherlands Indies and (Miss) Dr. C. Hyman, representing the Netherlands East Indies.

"(2) Dr. H. G. Morin, Directeur du Service du Paludisme en Indochine, Institut Pasteur de Saigon and Dr. Bader, Chemist of Malaria Service, representing French Indo-China.

"(3) Dr. A. Neave Kingsbury, Director, Institute for Medical Research, Kuala Lumpur and Dr. J. L. Rosedale, Professor of Biochemistry, College of Medicine, Singapore, representing British Malaya.

"Furthermore, this Committee shall be empowered to co-opt other workers experienced in this field of study so as to extend this investigation throughout the countries of the Far East."

W. F.

BRITISH MEDICAL JOURNAL. 1935. Mar. 23. p. 590.—The Malaria Epidemic in Ceylon. First-Hand Experiences.

The epidemic was due to a drought, which converted rivers into a series of pools.

Dr. WIGGLESWORTH has recently visited Ceylon, and in March he gave an address at the London School of Tropical Medicine and Hygiene on the subject of the epidemic in that island. He said that he felt that the Ceylon Medical Department had organized the distribution of quinine and the extension of the facilities for treatment with a rapidity and smoothness which had not received the commendation it deserved. The authorities sent sanitary inspectors round the districts and on the basis of their reports temporary centres had been established. The epidemic was mainly due to a drought which dried up the rivers until nothing remained but a series of pools in which *A. culicifacies* bred. The same drought which caused the malaria brought about failure of the rice crop with considerable destitution, and it was evident that relief would have to be undertaken on a more extensive scale. The town of Kurunegala, where antimalarial measures had been carried out for a number of years, was badly hit. Would it have been possible to prevent the epidemic? To have prevented the breeding of *A. culicifacies* over 300 miles of river and an indefinite area of streams by canalizing and oiling the pools would have been a far vaster undertaking than anything so far attempted for the control of malaria.

W. F.

DE SILVA (Stanley). Observations on Some Interesting Cases occurring during the Malaria Epidemic in Ceylon.—Jl. Trop. Med. & Hyg. 1935. Mar. 15. Vol. 38. No. 6. pp. 66-72. With 9 charts.

The author gives an account of the epidemic as he saw it in the wards of the General Hospital in Colombo. "The predominant parasite in

the epidemic was the malignant tertian parasite, and nearly 95 per cent. of the cases were so infected. [This statement cannot be applied to the epidemic as a whole, outside the hospital.]. . . The most characteristic feature of the epidemic was the frequency with which cerebral and nervous symptoms appeared. . . . Another striking feature was the slow pulse, particularly in the comatose cerebral and algid type of case, a pulse of 80 or 90 per minute with a temperature of 103° to 104°F was quite common." Gastro-intestinal symptoms were very frequent; nausea, vomiting, and watery stools with blood and mucus were seen in a large number of patients. These symptoms disappeared with malarial treatment. Many patients showed "pneumonic symptoms." All the patients with malignant malaria and cerebral symptoms had low blood-pressure. Intravenous quinine lowers the blood pressure still further; "this was responsible for the tragic results seen in the wards in cases treated with quinine intravenously, some patients dying soon after, and even during, the injection"; some were saved by adrenalin. Details are given of 13 illustrative cases of acute malaria.

W. F.

MCDONALD (W. M.). **The Malaria Epidemic in Ceylon.** [Correspondence.]—*Brit. Med. J.* 1935. May 11. pp. 1001–1002.

Dr. McDonald of Antigua, while admitting that it would have been impossible to have prevented the breeding of *A. culicifacies* in Ceylon by the usual methods of antilarval control, considers that it might be possible to prevent future epidemics by concentrating on the destruction of adult mosquitoes in the houses.

W. F.

COPELAND (A. J.). **The Muruts of North Borneo. Malaria and Racial Extinction.**—*Lancet.* 1935. May 25. pp. 1233–1239. With 11 figs. (2 maps).

The aboriginal Muruts are being exterminated by malaria.

The Muruts were formerly called "head-hunters" because they raided each other's villages to secure their enemies' heads. This is an affair of the past, and under wise guidance by European district officers they have become a docile, friendly people. They live in the dense jungle of the southern part of the interior of British North Borneo; they support themselves by hunting and fishing, and they number about twenty-two thousand. "Their debilitated physique is everywhere associated with highly endemic latent malaria," and their numbers have been steadily decreasing during the past eight years. Their neighbours, the Dusuns, on the other hand, are increasing. The Dusuns live in a more open environment in the upland plains and jungle of the north; they are husbandmen who keep cattle and grow rice. The author attributes the decline of the Muruts to malaria and he counsels that some £5,000 should be spent annually on quinine, instead of £57 as at present, and that the head tax of 2s. 4d. per annum should be abolished. The upsetting of the equilibrium between these primitive people and the jungle in which they live seems to have been due to the clearing of forest, and the introduction of virulent strains of malaria by labourers imported from Java.

W. F.

GREENFIELD (Gregor). Beitrag zur Frage der Malaria in Persien. [Malaria in Persia.]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. June. Vol. 39. No. 6. pp. 257-260.

A study of malaria as met with in Persia.

Malaria is the commonest disease in Persia. The author was stationed in the town of Malayer (Dowletabad), where the incidence of malaria amongst the population was over 20 per cent. Malaria was frequently complicated with pneumonia, pulmonary tuberculosis and dysentery. The diagnosis is often difficult as the symptomatology of malaria is very indefinite. Of 493 cases investigated 75 per cent. were benign tertian, 20 per cent. quartan and 5 per cent. malignant tertian. Purpuric symptoms were comparatively common: profuse bleeding from nose, haemorrhages under skin and mucous membranes, into muscles, also from the stomach, bowels and kidneys; the latter occurred in the severe cases. Scurvy could be excluded. More rarely cases of convulsion and coma occurred, and generally ended fatally. Quinine often failed even when given by injection. E. D. W. Greig.

CHAIKIN (V. I.) & ENIKOLOPOV (S. K.). A Short Epidemiological Description of Daghestan.—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1-2. pp. 142-147. [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. June. Vol. 23. Pt. 6. p. 167.]

"In Daghestan, malaria is rife and epidemics are favoured by the presence of large accumulations of water in irrigated rice-fields, swamps formed by small rivers and mountain streams, reservoirs in orchards, and neglected wells, filter pools, etc. The topography of 7 districts is discussed, with special reference to the breeding places of mosquitos and the prevalence of the disease. Of the Anophelines found in Daghestan, *Anopheles maculipennis*, Mg., was the most common and widely distributed. The adult males occurred from about the middle of May until the end of October. The larvae were found in all types of breeding place, but were most numerous in rather shallow water with a pH of 6.8-8 and a carpet of vegetation at the bottom. When larvicidal measures were carried out within a radius of 3 miles from some inhabited spot, the mosquitos bred in tubs and other receptacles for rainwater. *A. sacharovi*, Favr, which bred in places with dense tall vegetation rising above the surface of water, predominated in places where there was much subsoil fresh or mineral water. *A. hyrcanus*, Pall., came next in order of abundance, but *A. algeriensis*, Theo., was prevalent in some localities and, unlike the other mosquitos, sometimes occurred in shaded accumulations of water densely covered with reeds and having a peat bottom. *A. claviger*, Mg. (*bifurcatus*, auct.), *A. superpictus*, Grassi, and *A. plumbeus*, Steph., were rare."

LISOVA (A. I.) & ESKIN (V. A.). Infektion von *Anopheles maculipennis* var. *sacharovi* F. durch Malariaplasmodien in natürlichen Bedingungen in einem Reisfeldbezirk Uzbekistans. [The Infection with Malaria Parasites of *A. sacharovi*, Favr, under Natural Conditions in a Rice-cultivating Region in Uzbekistan.]—*Mag. Paras. Inst. Zool. Acad. Sci. U.R.S.S.* Leningrad. 1932. Vol. 3. pp. 49-62. With 4 figs. & 1 graph. [In Russian. German summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Feb. Vol. 23. Pt. 2. pp. 49-50.]

"This is an account of work carried out during a severe epidemic of malaria in July-November 1930 in a village of the Tashkent district.

Favourable breeding conditions for mosquitos are afforded by neglected rice-fields and by a defective irrigation system, vast expanses of water being formed, much of which is covered with dense vegetation. . . .

"Adults of *A. sacharovi* taken in dwellings were dissected after 4-6 days till the end of August, and after 8-10 days from September till November. Of 556 examined, 36 contained oöcysts or sporozoites, or both. The last infected mosquito was taken on the 18th September. The sporozoites usually occurred in the thorax and abdomen as well as in the salivary glands. The rate of infection was highest in August.

"In one instance no malaria parasites could be observed in the blood of patients suffering from primary malaria, whereas they were found in mosquitos taken in the same room. This suggests that the occurrence of the parasites in mosquitos might serve as supplementary data in diagnosis.

"Some of the mosquitos, particularly those taken in mosquito-nets in September, were infested with Nematodes, which were usually present in the Malpighian tubes and sometimes completely blocked them."

LANGTON (E. A. C.). **Some Observations on Infants and Young Persons in Bunyoro, Uganda.**—*East African Med. Jl.* 1935. Jan. Vol. 11. No. 10. pp. 316-325.

Quartan is the most common infection in infants. Benign tertian is very rare.

Sixty-five infants, none of whom showed any symptoms of malaria, were examined. Forty, 61.6 per cent., had enlarged spleens and 34, or 52.3 per cent., had parasites in their blood. Twenty-two were infected with *P. malariae* and 12 with *P. falciparum*. *P. malariae* was responsible for the largest spleens; this parasite became less common as the children grew older and was rarely seen after the age of 12. Among children under 5 years, 20 had quartan gametocytes in their blood, while only 2 had crescents. *P. vivax* was only found once in about 220 positive cases. There was a marked drop in the spleen rate after the age of 15.

W. F.

WILSON (D. Bagster) & WILSON (Margaret E.). **Infections with *Plasmodium ovale* Stephens, in Tanganyika Territory.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 469-474.

These cases of infection with *P. ovale* were found in natives during a survey made in the northern part of Tanganyika. Twenty-seven persons, among several thousand examined, were found to be infected with this parasite. Only one of the 27 was ill; this was a case of malarial coma due to a mixed infection with *P. ovale* and *P. falciparum*. Gametocytes are more frequently present and more numerous than in infections with other species.

W. F.

HANSON (Henry), BOYD (Mark F.) & GRIFFITTS (T. H. D.). **Some Factors in the Epidemiology of Malaria.**—*Amer. Jl. Public Health.* 1935. Feb. Vol. 25. No. 2. pp. 156-161. With 1 fig.

This concerns malaria in Florida.

The anopheles are: *A. quadrimaculatus*, *A. crucians*, two varieties (fresh and salt water), *A. punctipennis*, *A. atropos*, *A. walkeri*, *A. barberi*; all of them are potential vectors, but *A. quadrimaculatus* is far the most important. The greatest concentration of cases occurs in the northern counties, where the land is underlaid by limestone, and

where ponds, lakes and "sinks" are numerous. The spleen index taken in these regions, in 1931, was 25.6 per cent. The incidence is almost entirely rural. During the past 2 years (1932-34) 15,257 school children have been examined by the thick film method and 6.1 per cent. were found to be infected; 70 per cent. with subtertian, 21 per cent. with benign tertian, 0.2 per cent. with quartan. W. F.

BALFOUR (M. C.). **Malaria Studies in Greece. Measurements of Malaria, 1930-1933.**—*Amer. Jl. Trop. Med.* 1935. May. Vol. 15. No. 3. pp. 301-330. With 2 charts and 1 map.

A review of the published reports of malaria in Greece since 1905 indicates that epidemics of malaria recur at intervals. In 1930, there was a condition of low endemicity; in 1931, there was a severe epidemic; in 1932, there was a state of high endemicity; in 1933, a low stage of endemicity was reached once more. Since 1921, 5.6 per cent. of the total deaths in Greece have been caused by malaria. Quinine importations have varied from 20 to 50 tons annually. At ordinary times *P. vivax* and *P. malariae* are the common species of parasite, but *P. falciparum* takes the lead in epidemics. No major area in Greece is free from the disease. The spleen index, determined by the author, was 35.6, and the parasitic index 17.4; this was in 1933, a quiescent year of low endemicity. The rates were much higher in the small villages than in the towns. The relative percentages of the three species were: *P. falciparum* 38, *P. vivax* 34.5, *P. malariae* 26.5. The principal malaria season extends from the end of July to October. The seasonal wave in Greece is, on the average, longer, and continues later in the year than is the case in Italy and other European countries. It is believed that the explanation lies in the greater prevalence of *A. superpictus* in Greece. This anopheles has its greatest density in the autumn. W. F.

TRAUSMILLER (O.). Le paludisme dans les Iles de l'Adriatique: Krk, Rab et Pag. [**Malaria in the Adriatic Islands.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 291-303. With 2 maps & 2 figs. on 1 plate.

An example of control by means of *Gambusia* [see also this *Bulletin*, Vol. 30, p. 865].

The islands along the coast of Yugoslavia are malarious, while the mainland is comparatively healthy. The Dalmatian islands, on the contrary, are healthy while the mainland is malarious. The chief carrier in the three islands is *A. maculipennis*. In the island of Krk, there are no rivers and the rain sinks quickly into the porous soil, except in certain districts characterized as "red soil" districts. This red soil is less porous, and in these districts there are numerous ponds, or "lokvas" which furnish the sole supply of water for agricultural purposes. They become very foul through contamination by cattle, but nevertheless *A. maculipennis* breeds in them prolifically. *Gambusia* were first put into these lokvas in 1924, and they multiplied rapidly. The ponds were soon cleared of larvae, and the incidence of malaria was so much diminished that the distribution of quinine, which was formerly the principal method of combating malaria, became largely superfluous. In dry seasons many of the lokvas dry up and the fish perish; consequently owners have been made responsible for keeping their ponds clear of weeds and stocked with *Gambusia*.

The situation in the island of Rab which lies further south is quite different. Here there are numerous streams which come down from the hills and meander through marshy plains. Some drainage work has been carried out near the town, but treatment with drugs constitutes the principal method of dealing with malaria. Two years ago, treatment with atebrein and plasmoquine was introduced, and since then there has been a striking reduction in the amount of malaria.

In the island of Pag there are lokvas in the hills, and two brackish lakes in the marshy plains. Here again *Gambusia* has proved an efficient means of control, but if the *Gambusia* are destroyed, malaria returns; for example, the inhabitants sometimes throw the stems of a euphorbia into the lakes in order to stupefy the eels which then float to the top and are easily caught. Where this has been done, the *Gambusia* have been killed, anopheline larvae have thrived and malaria has increased.

W. F.

GIOVANNOLA (Arnaldo). *Plasmodium ovale* considered as a Modification of *Plasmodium vivax* after a Long Residence in the Human Host.—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 175–186. With 11 figs. [19 refs.]

The author does not accept *P. ovale* as a valid species.

This communication begins with a very useful critical survey of the cases of *P. ovale* infection which have been reported up to the present time, including the case reported by CRAIG in 1900. The author has compared the original Wagner-Jauregg strain of *P. vivax* with JAMES's strain of *P. ovale*, and he writes, "In conclusion the study of the Wagner Jauregg strain of *P. vivax* which has been passed for 15 years directly with blood from one man to another shows a parasite practically indistinguishable from the usual description of *P. ovale*. . . . *P. vivax* as we observed it in chronic infections and in inter-human passages is practically indistinguishable from the usual descriptions of *P. ovale*. . . . We must consider these modifications as due to the long residence in the vertebrate host in which the parasite had adapted itself by modifying its biology. . . . At present we have not enough proof to accept *P. ovale* as a fourth human *Plasmodium*."

W. F.

JAMES (S. P.), NICOL (W. D.) & SHUTE (P. G.). **The Specific Status of *Plasmodium ovale* Stephens.**—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 187–188.

The authors give the reasons why *P. ovale* is to be regarded as a separate species:—

(a) Its morphology differs from that of the other 3 species and the differences persist when the parasite is passed from person to person by direct blood inoculation.

(b) The character and arrangement of the pigment in the oocysts found on the stomach wall of the mosquito, 72 hours after feeding, is specifically diagnostic. The sporozoites are much smaller than those of *P. vivax*.

(c) The morphological character of the parasite, the periodicity of its asexual cycle in man, and the characteristic clinical course of the disease which it causes, are not altered by repeated passages through insect and human hosts.

(d) *P. ovale* is immunologically distinct from the other species of malaria parasites. Patients who are immune to all the three ordinary types are not immune to *P. ovale*.

(e) The clinical course of a first attack of malaria when it is due to *P. ovale* is different from a first attack due to one of the other species.

W. F.

STRATMAN-THOMAS (Warren K.). **Studies on Benign Tertian Malaria.**

8. **Observations on Splenomegaly.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 361-363.

These observations were made on patients who were given a single primary therapeutic infection with *P. vivax*. The conclusions reached were that (a) the degree of splenic enlargement is proportional to the duration of the primary attack. (b) After the cessation of the clinical attack, the spleen quickly decreases in size. (c) "If the clinical attack subsides but the maximum degree of splenomegaly persists there is possibility of a relapse." (d) Since splenic enlargement is transitory spleen surveys should be made at the height of the malaria season.

W. F.

BOYD (Mark F.), STRATMAN-THOMAS (W. K.) & KITCHEN (S. F.). **Studies on Benign Tertian Malaria. 9. An Instance of Natural Refractoriness in a Caucasian to Inoculation with *Plasmodium vivax*.**—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 364-365.

The patient, a white man who came from a place 95 miles from Tallahassee, was bitten on three occasions by numbers of mosquitoes of proved infectivity. The results were always negative. The strain used was the McCoy strain of *P. vivax*, which had its origin in a place within 12 miles of Tallahassee. The patient was then bitten by mosquitoes infected with the mild Steadman strain with the result that parasites were found in his blood 17 days later and persisted for 6 days in small numbers. There were no clinical symptoms and the temperature never approached 100°F. The patients had had three attacks of malaria during the previous six years. The authors conclude that this demonstrates the natural occurrence of homologous tolerance as well as some protection against heterologous strains.

W. F.

IYENGAR (M. O. T.). **Anophelines Infected with Malaria Parasites : a Further Note.**—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 371-372.

The author reported on a former occasion that he had found *A. jeyporiensis* James (type form) infected with malaria parasites under natural conditions in Travancore State, South India. He now amends this report and states that the infected specimens belonged to the variety *A. jeyporiensis* var. *candidiensis* Koidz. and not to the type form.

W. F.

HOWARD (H. H.), EARLE (W. C.) & MUENCH (H.). **A Method of Analysis of Field Malaria Data.**—*Jl. Amer. Statistical Assoc.* 1935. Mar. Vol. 30. No. 189A. Supplement. pp. 249-256. With 1 chart.

The data consist of (a) incidence of malaria, in numbers of cases per month; (b) intensity of mosquito breeding, in monthly average numbers of larvae and pupae per dipping period; (c) density of adult mosquito prevalence, in monthly average catches per animal-baited trap per night. The inquiry took place in Porto Rico and covers five years. A principal object of the report is to compare "inside," treated, zones with "outside" zones in six of the seven main areas of the island. The statistical method used may be illustrated on the data of monthly catches. From the experience of the five years a monthly trend was obtained and smoothed by a second order Fourier series. Then the expected values so obtained are subtracted from the individual monthly records, in order to reach indices freed so far as practicable from seasonal influence. The comparison of the residual systems of "inside" and "outside" showed a much greater rate of reduction in "inside" areas. It should be remarked that the fitted data are not actual numbers of mosquitoes caught but the natural logarithms of these numbers.

But, it might be objected that the dissimilarity of "treated" and "untreated" zones was due to the natural conditions in the latter being so unlike those of the former that no real control was provided. If this were so, then, after seasonal variations had been removed, there should be no significant correlation between fluctuations about the respective trend lines of the corresponding areas. Actually the correlation when time is held constant is increased. Further the correlation of different areas is insignificant (Luquillo and Santa Isabel). In 6 areas it was possible to compare "treated" and "untreated" zones with respect to the curve of captures; in three of these the difference in favour of the "treated" is, statistically speaking, highly significant, in two others about three times the probable error of the difference, in one not significant. Only two areas permitted of comparison on the basis of cases of malaria; in one the difference in favour of the "treated" was 2.9 times and in the other 3.7 times the probable error of the difference.

This is a carefully written and valuable piece of statistical analysis.

M. Greenwood.

PARROT (L.) & CATANEI (A.). Sur les renseignements fournis par l'indice splénométrique dans la mesure du paludisme endémique. [**The Splenometric Index in Endemic Malaria.**]—*Riv. di Malarologia.* Sez. I. 1935. Vol. 14. No. 1. pp. 32-34.

The splenic index is not a very good measure of the fluctuations of endemic malaria. Though the number of palpable spleens in a community may remain approximately the same, their sizes may alter owing to a decrease or an increase in the prevalence of malaria. The author measures all spleens in finger-breadths, reckoning from the costal margin. The palpable spleens of not more than 1 finger breadth are put in category 1. Those up to 2 finger-breadths in category 2, and so on up to 5 finger-breadths in category 5. All larger spleens are put in category 6. The figure for the average sized

spleen is obtained by adding all the category figures together and dividing by the total number of enlarged spleens. The figure thus obtained, multiplied by the splenic index, gives the splenometric index. Several examples illustrating the value of this index are given. For example, the splenic index of a labour force at Mitidja was 50.9 per cent., the splenometric index was 213. After 6 months' quinine treatment there was little alteration in the splenic index, which now stood at 48.1 per cent., but the splenometric index had fallen to 110, and indicated accurately the improvement which had taken place.

W. F.

SCHEMBRA (F. W.). Zur Frage der Kriegsmalaria. [The Question of War Malaria.]—*Deut. Med. Woch.* 1935. June 28. Vol. 61. No. 26. pp. 1044-1045.

Account from a Berlin hospital of a case of war malaria in which fever and death from another cause occurred 17 years later with malarial parasites in the blood.

A man of 48 had malaria in Macedonia in the European War. He had relapses at irregular intervals with rigors and quinine treatment till 1926 after which the disease disappeared. In 1929 he began to have pain in the belly attributed to the gall bladder. In 1933 the pain increased and he was removed in September to hospital, where operation was refused. A few days later he began daily rigors, his blood was examined and "plasmodia of tertian type were demonstrated in several blood smears and in thick drops." Four days later he died. Autopsy showed purulent cholelithiasis and "blackish pigmentation of the liver and spleen which were both enlarged." The author says that malaria acquired later or an autochthonous infection can be excluded. Cases, it is stated, have been recorded by RUGE and by DUMOLARD & AUBRY in which tertian relapsed after 10-17 years. The bearing on the pension question is briefly discussed. [See also p. 406, above.]

A. G. B.

KELLEY (W. H.) & SYDENSTRICKER (V. P.). Notes on Pernicious Malaria.—*Arch. Intern. Med.* 1935. May. Vol. 55. No. 5. pp. 818-825. With 1 chart.

This report reviews observations made on patients admitted to hospital with malaria in an area along the Savannah River in Georgia. The negro is more resistant than the white man, and although the population consists of an equal number of each, many more whites than blacks were admitted.

During a period of 15 years, 700 cases of severe malaria were observed—benign tertian 198, subtertian 502. The mortality was 0.5 per cent. for benign tertian and 9.98 for subtertian. Pernicious malaria occurred in 19.34 per cent. of the subtertian cases. It was more common in negroes than in whites. About half the cerebral cases died. Haemoglobinuria occurred in 16 persons, most of whom had suffered from repeated infections. Transfusion was employed for 12 such patients, 10 of whom survived. Fourteen had taken quinine shortly before the blackwater began, but no increase in haemoglobinuria was noted in 5 of those who received blood transfusion and were subsequently treated with quinine.

W. F.

SLATINEANU (A.), NICOLAU (S.) & BALMUS (G.). L'histopathologie du système nerveux dans le coma paludique. [**Histopathology of Nervous System in Malarial Coma.**—*Arch. Roumaines Path. Expér. et Microbiol.* Paris. 1935. Mar. Vol. 8. No. 1. pp. 5-43. With 24 figs. [47 refs.]

The authors give a comprehensive view of the work which has been published, especially as regards Dürck's nodules. They then describe very fully their own findings in a fatal case of malarial coma. The paper is illustrated by a number of drawings.

They found an acute polynuclear inflammation of the meninges with some oedema of the membranes; swelling of the nerve cells with chromatolysis of Nissl's granules; glial proliferation; a parenchymatous mononuclear infiltration, which sometimes gave rise to nodules; vascular lesions such as thrombosis, haemorrhage, and inflammation within and around the vessels; malarial pigment in the connective tissue cells, endothelium, meninges, etc. Malarial pigment was not found within the neurones, but the authors describe a "*brown pigment*," which was very abundant there, especially in the nerve cells where it sometimes obscured their structure completely. This brown pigment contained no iron, was not doubly refractive like malaria pigment, and was neither a carotene nor a chromolipoid. Lesions in the peripheral nervous system were most marked in the spinal and plexiform ganglia. In the nerve-roots and in the nerves themselves, interstitial inflammation and perivascular changes were present.

W. F.

TIRUMURTI (T. S.) & RADHAKRISHNA RAO (M. V.). **The Rôle of Malaria in the Causation of Cirrhosis of the Liver—a Preliminary Note.**—*Jl. Indian Med. Assoc.* 1935. Apr. Vol. 4. No. 8. pp. 315-317. [18 refs.]

The authors are "convinced from experience in South India that malaria *per se* is not a direct cause of cirrhosis of the liver." They have collected livers from cases of chronic malaria, and will report on them later.

W. F.

SALEUN (G.) & MONIER (H. M.). Renseignements et techniques particulières recueillis à l'école italienne de malariologie. [**Lessons learnt in the Italian School of Malariology.**—*Ann. de Méd. et de Pharm. Colon.* 1934. Oct.-Nov.-Dec. Vol. 32. No. 4. pp. 472-493.

Useful notes on the testing of Paris green, reticulocytes, precipitin tests, Alessandrini's theory of macroptera and rice-fields, immunity in malaria, etc.

The authors here set out the contents of their notebooks compiled in Italy. They cover a wide range of subjects, from theories about the origin of blood corpuscles to the staining of malaria parasites. Under the heading of Paris green, they say that if this is too fine it binds into lumps and cannot be spread, while if it is too coarse it cannot be taken up by the mosquito larvae. Paris green is often adulterated with baryta. In order to detect this, put a little into a test tube containing 5 cc. of ammonia. If the Paris green is pure, the ammonia turns blue and remains clear; but if it contains baryta,

it becomes cloudy. In order to test if the labourers are applying Paris green regularly, take 10 cc. of the water from the surface; put it in a flask with some small pieces of zinc and a little dilute sulphuric acid; put a piece of filter paper over the mouth of the flask, with a little powdered silver nitrate on the top of it. After a few minutes—if the water contains any Paris green—the silver nitrate becomes first yellow, then brown, and, if one adds a drop of water, black. [But all traces of arsenic disappear very quickly after dusting with Paris green.]

The method of Cesaris-Demel for the intravital staining of reticulocytes is described. The following stain is employed:—

Brilliant cresyl blue	2 gram.
Soudan III	4 "
Absolute alcohol	15 "

A perfectly clean slide is warmed slightly, and two drops of this stain are allowed to fall on it. This evaporates and forms a thin coloured film. A drop of the blood to be examined is taken on a cover slip, and this is dropped wet on to the coloured slide. When reticulocytes are scarce they may be concentrated by centrifuging in sodium citrate. Under the plasma in the centrifuge tube, and above the red corpuscles, comes the grey layer. In this grey layer are found, in the following order:—the white cells, the megaloblasts, the red cells containing malaria parasites. Technical notes in connexion with many other investigations are given, for example: precipitin testing of mosquito blood meals; methods of storing live mosquitoes; Barber's rapid method of examining salivary glands; the mounting of mosquitoes' stomachs and salivary glands, etc. Professor Guglio ALESSANDRINI's theory of macropteris and micropteris anopheles is mentioned. He looks upon malaria as primarily a disease of the small weak microptera which breed in the marshes where their food is protozoa. The large, strong macroptera which breed in the rice-fields and feed on nourishing plankton consisting of algae, can resist infection with the parasites of malaria. ALESSANDRINI therefore recommends planting rice as an anti-malarial measure. The work of SCHILLING and NEUMANN in connexion with immunity in trypanosomiasis and malaria is also mentioned. Possibly the process is as follows:—antibodies are produced at the first attack and destroy all but a few parasites. Those few, resistant parasites gradually increase until they cause another attack, and produce a second lot of antibodies different from the first. Again a few parasites escape which produce a third lot of antibodies; and so on until "the accumulation of different antibodies creates a progressive premunition." W. F.

VAN NITSEN (R.). Essai de prophylaxie rationnelle chez l'enfant indigène. [**Rational Prophylaxis in the Native Child.**]*—Bull. Méd. du Katanga.* 1934. Vol. 11. No. 6. pp. 185, 187–193.

All the native women in the Panda camp are taken into hospital for their confinements and, subsequently, they bring their babies every day to the infant-welfare centre until they are a year old. Afterwards the children are given a free meal every day in the camp canteen until they are two years old. Once a month, the blood of the children is examined by the thick film method, and those with parasites are given treatment for six days. This brings about a great improvement in the health of the children, and reduces the numbers infected with gametocytes, but it does not get rid of the children's

malaria entirely, and consequently it does not interfere with the development of immunity. The doses given were as follows:—Children up to 6 months, 5 centigrams of atebtrin daily; children from 6 months to 2 years, 10 centigrams daily. The doses of plasmoquine for the same ages were one-tenth of the doses of atebtrin.

W. F.

GAIGNAIRE. Confusion mentale, mélancolie anxieuse et mélancolie délirante curable, d'origine paludéenne. [**Mental Confusion in Malaria.**—*Ann. de Méd. et de Pharm. Colon.* 1935. Oct.–Nov.–Dec. Vol. 32. No. 4. pp. 572–574.

The delirium of malaria usually disappears with the falling of the temperature, but the author describes three cases of pernicious malaria in natives of the Bakaka tribe, where the delirium passed into a state of mental confusion in which the hallucinations of the delirium persisted, and the patients remained in a state of terror from which they could not be aroused, but continued to groan, lament and cry out in fear. The symptoms passed off during convalescence. Three other cases from the same tribe were brought to the author suffering from mental symptoms of some months duration. Their mental state was characterized by anxiety, they groaned and lamented and accused themselves of grievous sins. Their spleens and livers were enlarged, parasites were present in the blood, and complete recovery followed anti-malaria treatment.

W. F.

DJAPARIDSE (P. S.). Ueber die Frage der Malariaödeme. [**Malarial Oedema.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. June. Vol. 39. No. 6. pp. 252–256.

A study of the disturbances of the water metabolism in malaria.

The author investigated the problem in 117 cases of malaria in Suchum [? Georgia, on the Black Sea]. Of the 117, 13 were infected with *Plasmodium vivax*, 79 with *Plasmodium malariae* and 25 with *Plasmodium falciparum*. Oedema occurs most frequently in cases of quartan malaria, less frequently in malignant tertian and least in benign tertian. If there are kidney lesions albuminuria with casts is present, but there may be oedema without albuminuria. The cause of oedema without albuminuria, particularly frequent in quartan malaria, is not clear and requires further investigation; possibly endocrines may play a part. The cases of oedema without albuminuria are easily cured by quinine, and this is important in the differential diagnosis. Since cases may occur in endemic areas without showing typical signs of a malarial attack it is essential to make extensive blood investigations including the melanoflocculation reaction.

E. D. W. Greig.

CORMAN (A.). Hémorragie sous-capsulaire de la rate au cours d'un accès aigu de malaria. [**Rupture of the Spleen during an Acute Attack of Malaria.**—*Bull. Méd. du Katanga.* 1935. Vol. 12. No. 1. pp. 22–25.

The rupture of an enlarged spleen during vomiting caused terrible pain and great tenderness.

The patient, a man of 32, had suffered from several attacks of malaria during the course of the two years preceding his admission to hospital. During an acute attack, he vomited violently after quinine, and, while he was retching, he was seized by a sudden pain in his left side so severe that he fainted. He was admitted to hospital with all the signs of abdominal haemorrhage and an exquisitely tender area over the left side of the abdomen, in which there was a localized area of dullness and swelling in the position of his enlarged spleen. A haemorrhage under the splenic capsule was diagnosed. He was treated with coagulant drugs and the local application of ice, and he recovered. An attack of blackwater, with malaria parasites in the blood, occurred during his convalescence and was treated with atebtrin.

W. F.

BARBOSA (Amando). La quinina y la atebrina en la prevención de las recrudescencias que siguen a la recurrencia de terciana benigna. (Estudio comparativo.) [**Quinine and Atebrin in preventing Recrudescences after Recurrence of Benign Tertian Malaria.**]—*Medicina Países Cálidos*. Madrid. 1935. Mar. Vol. 8. No. 3. pp. 139–144.

The author follows JAMES in defining a "recrudescence" as a return of fever and parasites within 8 weeks of recovery from the primary attack; a "relapse" as a return between 8 and 24 weeks, and a "recurrence" as a return at some time later than 24 weeks (see this *Bulletin*, Vol. 28, p. 567). He treated 49 patients suffering from benign tertian with quinine and another 49 with atebtrin. In each group there were 12 adults and 37 children. The dosage of atebtrin was 0.1 gm. daily for children between 6 months and 5 years; from 5–9 years 0.15 gm., 10–12 years 0.2 gm. and over 12 years 0.3 gm. The dose of quinine was also graded, the usual dose for an adult being 1 gm.

Each patient was kept under observation for a period of two months after recovery from the recurrence. Seven recrudescences occurred among the 12 adults treated with quinine or 58.3 per cent. [The percentages are stated for purposes of readier comparison, with the known proviso of the fallacy of calculating percentages on small numbers.] There were five among adults treated with atebtrin, or 41.6 per cent. Among the 37 children given quinine there were 18 recrudescences, *i.e.*, 48.6 per cent., and among those treated with atebtrin 14 or 37.8 per cent. Taking adults and children together, there were 25 recrudescences among the 49 treated with quinine and 19 among the atebtrin group or 51 and 38.7 per cent. respectively. In other words, atebtrin is more effectual than is quinine in preventing recrudescences following recurrence of benign tertian, both in children and adults.

Again, the average period before the recrudescence in those treated with quinine was 20.4 days, in those treated with atebtrin 41.7 days; that is, atebtrin delays the appearance of the recrudescence, the interval being fully double the length of that of the quinine treated group.

H. H. S.

- i. MORISHITA (Kaoru), MIYAHARA (Hatsuo) & ISHIOKA (Hiozo). **Studies in the Treatment of Malaria XIII. Experimental Treatment with Plasmoquine and Atebrin as carried out by our APA Method.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1935. Mar. Vol. 34. No. 3 (360). [In Japanese pp. 319–328. [14 refs.] English summary pp. 328–330.]
- ii. —, — & —. **XIV. Further Notes on the Experimental Treatment with Plasmoquine (5th Report). On a Modified Use of Plasmoquine (PQB Method).**—*Ibid.* [In Japanese pp. 338–346. English summary pp. 346–348.]

i. Twenty-one patients were given 0.3 gram atebrin and 0.03 gram of plasmoquine daily for seven days. They were kept under observation for 8 weeks, and none of them relapsed. The duration of parasites after the beginning of treatment was: benign tertian, 1 to 3 days; quartan, 1 to 4 days; crescents, 1 to 8 days; subtertian trophozoites, 1 to 3 days. The authors call this method of treatment the A.P.A. method.

ii. Twenty-two patients were treated by the P.Q.B. method which consists of 0.9 grams of quinine daily for 2 weeks, with 0.04 grams of plasmoquine in the first week. The patients were observed for 8 weeks. There was a relapse rate of 23 per cent. in benign tertian, and 15 per cent. in subtertian. W. F.

CIUCA (M.), FRANKE (M.) & ALEXA (E), with the collaboration of C. AGAPI, E. PUPU & E. MANOLIU. Contribution à l'étude de l'efficacité thérapeutique comparée de l'atébrine seule ou associée avec d'autres produits antipaludéens dans l'infection naturelle. [**Comparative Study of Treatment by Atebrin Alone and Associated with Other Drugs.**]—*Arch. Roumaines Path. Expér. et Microbiol.* Paris. 1935. Mar. Vol. 8. No. 1. pp. 111–123. With 3 figs.

The authors treated 110 patients for a period of 7 days with daily doses of one of the following—

(a) atebrin	0.30 ctgr. (? gram)
(b) atebrin	0.30 + plasmoquine 0.02
(c) atebrin	0.30 + quinine 0.50
(d) quinine	1 gram
(e) quinine	0.50 + plasmoquine 0.02

There was no apparent difference between quinine and atebrin in the treatment of the attack. Atebrin and quinine together were not superior to either drug given separately. Combined treatment with atebrin and plasmoquine often produced toxic symptoms; this combination should be used only under strict observation by a medical man. Staining of the skin in cases treated with atebrin tended to be more marked in severe cases. W. F.

BIGGAM (A. G.). **Atebrin and Malaria.**—*Jl. Roy. Army Med. Corps.* 1935. June. Vol. 64. No. 6. pp. 400–402.

Four European soldiers who had been treated with quinine and plasmoquine in the tropics, suffered from benign tertian relapses on their return to England and were treated with atebrin 0.3 grams daily for five days. Three of them relapsed in about 5 weeks and one in 14 weeks. W. F.

KIRILOV-DRENOWSKY (A.). Orientierende therapeutische Versuche mit der 6-Tage-Behandlung mit Atebrin, Atebrin + Plasmochin-simplex, Plasmochin-compositum, Chinoplasmin und Chinin. [**Comparative Therapeutic Observations on a 6-Day Treatment with Atebrin, Atebrin + Plasmoquine Simplex, Plasmoquine Co., Quinoplasmoquine and Quinine.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. June. Vol. 39. No. 6. pp. 243-252.]

The title of this paper indicates its scope.

The observations were made in Bulgaria in a heavily infected village in the district of Plovdiv. In May 1934 the splenic index was 82·8 per cent. and the parasite index 18·8 per cent. The treatment was begun on 27th May 1934 and ended on 5th October 1934. The nature of the infection amongst the patients was :—*Plasmodium vivax* in 78 persons, *Plasmodium malariae* in 2, *Plasmodium falciparum* in 31, and mixed in 4. The ages varied from under 1 year to over 15 years. The drugs were given in the usual doses with appropriate reductions for children of various ages. The atebrin plasmoquine-simplex combination was used in a proportion 10 : 1. Toxic symptoms were noted in some cases, chiefly abdominal pain and cyanosis of lips. As a result of the observations the author concludes that :—for a 6-day treatment the method of choice is the atebrin plasmoquine combination, it gave only a 3·7 per cent. of relapses. He puts next the atebrin treatment alone, it is remembered that young children require correspondingly higher doses. In the third place he brackets equal, quinine with a 25 per cent. relapse rate, quinoplasmoquine with 33 per cent., and plasmoquine co. with 42 per cent. of relapses. [The groups contained from 21 to 27 persons each.]

E. D. W. Greig.

BLAZE (John R.) & SIMEONS (A. T. W.). **Preliminary Observations on a New Soluble Atebrin Compound.**—*Indian Med. Gaz.* 1935. Apr. Vol. 70. No. 4. pp. 185-188. With 21 charts.

This is an important report on 21 cases of malaria treated very successfully with intramuscular injections of atebrin musonate.

It is a yellow, easily-soluble powder, put up in dry ampoules, each containing 0·125 grams (corresponding to 0·1 gram of atebrin dihydrochloride) to be dissolved in exactly 3 cc. of water before use. The doses recommended by the makers are 1 ampoule for intravenous injection, or 3 ampoules for intramuscular injection. According to HECHT (this *Bulletin*, Vol. 31, p. 171) atebrin is absorbed in the duodenum, and taken to the liver; thence it is excreted with the bile back into the duodenum to pass once more back to the liver with the portal blood. According to this theory, very little atebrin reaches the general circulation until the liver has been saturated with it, and this explains why none appears in the urine until treatment has been continued for several days. Theoretically then, atebrin should act much more promptly when it is injected.

The results were as follows :—A single intramuscular injection of 0·375 grams sometimes had a remarkable effect, but a recrudescence usually occurred within a few days. Two injections given on successive days were sufficient to get rid of all asexual benign tertian and subtertian parasites within 4 days; occasionally, parasites reappeared after a few days, but they disappeared spontaneously. The injections were painless, and there were no toxic symptoms. The intravenous route, though harmless, is not satisfactory for routine treatment. W. F.

SLATINEANU (A.) & SIBI (M.) with the collaboration of M. FRANCKE, E. VEIT, E. LUPU & Z. PARASCHIVESCU. Exploration fonctionnelle du foie et du rein dans le paludisme, avant et après traitement à l'atébrine pure ou combinée avec plasmoquine ou quinine. [**The Liver and Kidney in Malaria and after Atebrin Treatment.**]—*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1934. Dec. Vol. 7. No. 4. pp. 529–543. [32 refs.]

The yellow colouration of the skin produced by atebrin is a danger sign, and patients showing it should be watched carefully. It appears to be associated with defective action of the liver and kidneys. Atebrin should not be employed except under medical supervision. Before treatment, a transitory hepatic insufficiency was found in all the 60 cases of malaria examined; it was less marked in benign tertian; acidosis was associated with it in many cases. No great reduction of chlorine or great azotaemia were found. A moderate renal insufficiency was found in subtertian and quartan. W. F.

SONI (R. L.). **A Note on Yellow Discoloration in Atebrin Therapy.**—*Indian Med. Gaz.* 1935. Apr. Vol. 70. No. 4. pp. 211–212.

Atebrin pigmentation never occurs before the third day. Slow excretion and cumulation are important factors, but constipation, intercurrent infections, etc., also modify the intensity and duration of the discolouration. The author gives details of a case in which pigmentation persisted for three months, and he ascribes the unusually long duration to a streptococcal infection of the throat from which the patient was suffering. W. F.

STORM (C. J.). Ueber die Anwendung des Suprarenins bei intravenöser Injektion von Atebrin im Affenversuch. [**Use of Adrenalin in Intravenous Injections of Atebrin to Monkeys.**]—*Klin. Woch.* 1935. May 25. Vol. 14. No. 21. pp. 756–758. With 3 text figs. [13 refs.]

An experimental study on the control by adrenalin of the toxic symptoms produced by intravenous injections of atebrin.

The author carried out his experiments on monkeys. Intravenous injection of atebrin has a marked effect on the circulation evidenced by a pronounced drop in blood pressure, also by irregularities in the rhythm of the pressure curve due mostly to extra systoles. The author showed by his experiments that this fall in pressure could be prevented by adrenalin and for this and other reasons he recommends the use of adrenalin with intravenous injections of atebrin.

E. D. W. Greig.

i. HECHT (Gerhard). Experimentelle Untersuchung von Zirkulationsstörungen durch Plasmochin und Atebrin. Erwiderung auf die Arbeit von de Langen und Storm. [**Experimental Investigation of Circulatory Disturbance by Plasmoquine and Atebrin. Reply to de Langen and Storm.**]*—*Klin. Woch.* 1935. Vol. 14. pp. 714–716. [16 refs.]

ii. EICHHOLTZ (F.). Bemerkungen zur Arbeit von de Langen und Storm. [**Notes on the Work of de Langen and Storm.**]—*Ibid.* pp. 716–718.

[The opportunity—denied to most European laboratories—of using monkeys as test animals is fully taken advantage of by workers in

* DE LANGEN & STORM's article was reviewed on page 418.

the Dutch East Indies and there is little doubt of the importance and utility of such experiments, especially in pharmacology. It was, however, only to be expected that emphasis of the complications which may follow the use in man of the most important antimalarial synthetic drugs of recent times, atebtrin and plasmoquine, based on monkey experiments, should elicit a reply from those who have used mainly the smaller laboratory mammals for test. The subject is a very important one for tropical practitioners and we may, without passing any judgment on the controversy, extract the opinions of those who are well qualified to express them.]

i. Hecht questions the claim that monkeys are ideal test animals and attributes the supposed great susceptibility of the monkey heart to atebtrin as due rather to the ill-advised perfusion method employed. Again, he considers that parenteral injection of a test drug cannot furnish a criticism of its suitability for oral administration. This is especially the case for intravenous injection. He is convinced too, that intramuscular injection in monkeys has just the same action as in cats. With these latter animals he could discover no effect upon respiration and circulation of even 20 mgm. atebtrin per kgm. by intramuscular injection, although a negative variation of blood pressure could be obtained with a dose intravenously of 2 mgm. per kgm. Such an effect then could only be expected in man by intravenous injection. There is, however, no indication at all for intravenous injection of plasmoquine for its gametocidal effect. There are rare occasions, however (malarial coma) where urgency demands immediate action upon malarial schizonts and here the choice must lie between intravenous administration of atebtrin or quinine. Tropical practitioners have already used the tablets of atebtrin, intended for oral administration, for this purpose and have found that intravenous doses of 0.2 gm. atebtrin—corresponding to 3 mgm. per kgm.—have been seldom followed by any complication. Evidently the dose recommended for intravenous injection is to be of the order of 0.1 gm. Such a dose would seem to come within the limit of safety as laid down by DE LANGEN for man. Such a man, “of 50 kilogram., in good bodily condition, with a blood pressure not lower than 100 mm. could probably stand an intravenous dose of 200 mgm. atebtrin.” The position reduces to this, that both atebtrin and quinine have their dangers, when used by intravenous injection and the choice is left by the author to the practitioner whether he will select for intravenous inoculation an intravenous dose “of 0.1 gm. atebtrin (which may be repeated 2 or 3 times without danger, as is shown by animal experiment, at intervals of an hour) or an effective dose of quinine.”

ii. The main complications to be expected from the action of plasmoquine are disturbance of cardiac rhythm and formation of methaemoglobin. But in the case of man very much smaller therapeutic doses are necessary than are capable of producing these effects, especially the doses that are used at the present time, which have diminished from the original 0.06 to 0.02 or 0.03. The author is not in favour of the combination of adrenalin, which has its own dangers, with plasmoquine nor yet of combining quinine and plasmoquine in intravenous injection.

W. F. Harvey.

WATS (R. C.) & GHOSH (B. N.). **Quantitative and Qualitative Methods for Detection of Atebrin in Urine.**—*Records of the Malaria Survey of India*. 1934. Dec. Vol. 4. No. 4. pp. 367–370.

The technique of the qualitative test is as follows ; those wishing to carry out quantitative tests should consult the original :—

" (1) About 100 c.c. of the urine containing atebrin are rendered alkaline with 10 gm. of potassium carbonate, and shaken with 20 c.c. of amyl alcohol in a glass cylinder.

" (2) The supernatant alcohol layer is poured off from the top, and, if turbid, is washed with a saturated aqueous solution of potassium carbonate.

" (3) The presence of atebrin would be evident from the typical yellow colour imparted to amyl alcohol, and can be confirmed in the following way. With a convex lens the bright sunlight is focused against a black background and the tube containing the extracted amyl alcohol interposed in a slanting position between the lens and its focus. A distinctly green fluorescence is noticeable in the beam of light, especially on moving the lens parallel to the tube. It should be distinguished from the faint blue fluorescence sometimes caused by the solution of urobilin in amyl alcohol.*

" The green fluorescence, mentioned above, is quite distinctly shown in an amyl alcohol extract containing atebrin in dilutions up to 1 in 2,000,000. This last would correspond to the presence of atebrin in a dilution up to 1 in 10,000,000 in the urine tested."

W. F.

BLACKIE (W. K.). **A Fatal Case of Plasmoquine Poisoning.**—*South African Med. Jl.* 1935. Mar. 9. Vol. 9. No. 5. pp. 147–148.

" The tragic termination of this self-treated case points clearly to the need for medical supervision in all cases of plasmoquine therapy."

The deceased had twice suffered from blackwater, and each time the attack had followed a small dose of quinine. Three days before his death, he felt seedy and obtained plasmoquine and atebrin from a chemist. In the following 24 hours, he took 0.6 gm. of atebrin and 0.03 gm. of plasmoquine, after which he complained of a tightness about the throat and respiratory distress. He continued with the drugs and, on the second day, he took the same doses as on the first. He then complained of griping pains in the abdomen, together with difficulty in breathing, swallowing and speaking. His temperature had risen to 102°F. and his lips were blue. He died on the following morning. No signs of recent malaria were found post mortem. Cyanosis was present in the finger-nails, the ears, lips, gums and palate. The kidneys were intensely congested and swollen ; they presented the appearance of acute haemorrhagic nephritis. The liver was soft, " suggestive of . . . parenchymatous necrosis." The highly acid urine contained methaemoglobin, granular casts, granular debris, and numerous leucocytes.

W. F.

HICKS (E. P.) & CHAND (Diwan). **The Relative Clinical Efficacy of Totaquina and Quinine.**—*Records of the Malaria Survey of India*. 1935. Mar. Vol. 5. No. 1. pp. 39–50.

The authors found that quinine and both types of totaquina were

* " We have found that if one drop of pure sulphuric acid be added to every c.c. of the amyl alcohol extract, and the mixture be heated in a boiling-water bath for 3 minutes, the blue fluorescence due to urobilin is eliminated. The specimen should, however, be examined while still hot, as some turbidity appears on cooling.

" The addition of quinine salts, salicylates, caffeine, plasmoquine or iron salts to the urine has not been found to interfere with the green fluorescence characteristic of the amyl alcohol extract containing atebrin."

of equal efficacy in the immediate cure of malaria, and that there was no appreciable difference in their toxicity.

They treated 210 prisoners suffering from benign tertian and 158 suffering from malignant tertian. The drugs used were (a) quinine; (b) totaquina Type I which contained 32 per cent. quinine and 11 per cent. cinchonine; (c) totaquina Type II which contained 19 per cent. quinine and 20 per cent. of cinchonine. The doses were 0.6 gm. daily per 70 kgm. of body weight in benign tertian, and 1.2 gm. daily in subtertian. The drugs were given in tablets. The patients had been exposed to malaria all their lives. The mean duration of parasites, under treatment with any one of the three drugs, was less than 1.5 days; the mean duration of fever was less than 2 days. Parasites and fever disappeared rather more quickly with totaquina Type II; "in most cases the differences between the drugs are small and are within the limits of error due to random sampling." The authors "suggest that a dose of 1.0 gm. or 15 grains once daily for 3 or 4 days would be suitable for the routine treatment of rural populations in the Punjab. This should be large enough to prevent the majority of deaths and to remove the clinical symptoms, which is all that is demanded by such populations." [See pp. 114 and 410, above.]

W. F.

PÂRVULESCU, CONSTANTINESCO (N.) & BOERIU (V.). Efficacité comparée du totaquina dans le paludisme humain (infection naturelle). [**Totaquina in Malaria. Comparative Worth.**]—*Arch. Roumaines Path. Expérim. et Microbiol.* Paris. 1934. Dec. Vol. 7. No. 4. pp. 523-528.

Comparative tests were made with two samples of totaquina, Type I; with two samples of totaquina, Type II; and with quinine sulphate. The tests were made upon 213 young soldiers who were in hospital suffering from malaria. Benign tertian patients were given 0.6 gm. (9 grains) daily for 5 days; subtertian and quartan cases were given 1.2 gm. (18 grains). These small doses were employed in order to bring out the difference in the efficiency of the several drugs; when double these quantities were given they were all equally effective. The results showed that a Type I totaquina, or a Type II totaquina which has been brought up to the same standard, acted as well as quinine; but, in the small doses used, a Type II totaquina, of which more than 50 per cent. of the alkaloids consisted of cinchonine, was less efficient.

W. F.

PINELLI (Luigi). La terapia cacodilica ad alte dosi nella malaria acuta e cronica. [**Sodium Cacodylate in the Treatment of Malaria.**]—*Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 2. pp. 136-145. French summary.

The author states that sodium cacodylate causes no inconvenience, has no effect on the temperature nor any destructive action on the asexual forms. The enlargement of the spleen is little if at all reduced and that little only if the enlargement is recent. It does however improve the general condition, especially in chronic malaria, increases the body weight, restores the blood to normal and effectively enhances the action of the quinine.

Fifteen patients suffering from acute malaria, primary or relapse, and 20 suffering from chronic forms of the infection were treated with large

doses. The drug was made up of a strength of 0.25 gm. in 1 cc. with distilled water. In acute cases 0.3–1.5 gm. were given daily for 10 days, either intramuscularly or intravenously. In chronic cases the course was spread over 20–30 days, including days of intermission in administration; thus: For the first two days 2 cc. morning and afternoon = 1 gm. of the drug in the day. This was followed by two days' rest. On the next three days 2 cc. were injected in the morning, at midday and in the evening, *i.e.*, 6 cc. or 1.5 gm. of the drug; 3 days' rest. For the next five days 4 cc. morning and evening = 2 gm. in all, and after another 5 days' rest, injections daily for 5 days of 4 cc. morning, midday and evening. [The author calls this a total of "2.5 gm. of cacodylate in the day," but 12 cc. would contain 3 gm.] At the morning dose 1.4 gm. quinine [? salt] is given *per os*. Two courses with an interval of 20 days suffice to cure. *H. H. S.*

SAUTET (Jacques). Contribution à l'étude du paludisme chez les enfants. Les traitements nouveaux. [**Treatment of Malaria in Children.**]—*Rev. Méd. et Hyg. Trop.* 1934. Nov.–Dec. Vol. 26. No. 6. pp. 257–261.

The author gives a table of the doses of acridine and quinoline derivatives recommended for children.

He stresses the importance of treating children, because they are the chief reservoirs of infection. He begins treatment either with quinine, or with one of the acridine derivatives, *i.e.*, with atebrin or quinacrine which are identical substances. A useful method for children is to conceal the tablet in a raisin. The doses recommended are:—

0 to 6 months	quinine is preferable.
6 months to 1 year	0.025 gram acridine derivative daily for 4 days.
1 year to 2 years	0.05 " " "
2 years to 4 years	0.10 " " "
4 years to 8 years	0.15 " " "
8 years to 10 years	0.25 " " "
10 years to 15 years	0.30 gram acridine derivative daily for 5 days.

The daily amount should be given in 2 or 3 doses.

This treatment should be followed by treatment with one of the quinoline derivatives—plasmoquine (Bayer), rhodoquine (Poulenc-Rhone), plasmoquine (Russian)—in order to destroy the gametocytes. These drugs are easy to give because they are not bitter like the acridine derivatives, but they are toxic. The doses recommended are:—

0 to 6 months	0.0025 gram.
6 months to 2 years	0.0050 "
2 years to 4 years	0.0075 "
4 years to 8 years	0.0100 "
8 years to 10 years	0.0150 "
10 years to 15 years	0.0200 "

These doses are given twice a week for 6 months.

W. F.

PITTALUGA (G.). Die Behandlung der Malaria. (Zusammenfassung der Erfahrungen spanischer Malariologen.) [**Treatment of Malaria in Spain.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. July. Vol. 39. No. 7. pp. 291–296.

The experiences of Spanish malariologists in the treatment of malaria.

The problems with which they had to deal were :—1. The treatment of acute primary cases of the three types. 2. The treatment of relapses of long and short duration. 3. The treatment of chronic and latent cases with general and visceral symptoms, splenomegaly, anaemia, etc. 4. The treatment of abnormal forms of the disease, mixed infections, blackwater fever, quinine idiosyncrasy.

The author considers the most satisfactory scheme of treatment is a 7-day treatment with atebirin in the usual doses followed by a course of plasmoquine. At end of this course an after treatment with quinine and arsenic for 14 days is advised. He recommends the parenteral treatment with adrenaline as a supplementary therapy for the asthenia which accompanies many cases of malaria. *E. D. W. Greig.*

- ALESSANDRINI (G.). Nuove vedute sulla biologia dei parassiti malarigeni. *Atti V. Congr. Naz. Microbiol., Cagliari 27-31 Maggio 1934.* pp. 17-37. [See this *Bulletin*, Vol. 30, p. 734.]
- ARIMA (I.). Beitrag zur Malaria-Serumreaktion (Melanoflockulation).—*Fukuoka Acta Med. (Fukuoka-Ikwadagaku Zasshi).* 1935 June. Vol. 28. No. 6. [In Japanese. German summary pp. 61-62.]
- BALDI (Americo). Malaria autoctona nel comune di Pistoia. Nota preventiva.—*Riv. di Malarologia. Sez. I.* 1935. Vol. 14. No. 1. pp. 42-44. French summary (6 lines).
- BENARROCH (E. I.). A propos de la réaction de Henry pour la diagnostic du paludisme.—*Riv. di Malarologia. Sez. II.* 1934. Vol. 13. No. 6. pp. 329-341.
- BOURGIN (P.). Un cas d'hémorragie intestinale palustre à Soctrang.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Feb.-Mar. Vol. 13. No. 2. pp. 139-141.
- CANAVAN (Wm. P. N.). Present Status of Malaria in Oklahoma.—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 225-230. With 3 figs.
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- COPELAND (A. J.). Malaria and Racial Extinction. [Correspondence].—*Lancet.* 1935. June 22. p. 1472.
- FICACCI (Luigi). Emoglobinuria da plasmochina.—*Policlinico. Sez. Prat.* 1935. Jan. 28. Vol. 42. No. 4. pp. 136-139.
- GREENFIELD (Gregor). Ein Fall von Malaria mit Mastitis.—*Arch. f. Schiffsu. Trop.-Hyg.* 1935. Aug. Vol. 39. No. 8. pp. 347-348. [See this *Bulletin*, Vol. 13, p. 72.]
- HAUER (August). Ueber Chininintoxikation und Chininidiosynkrasie.—*Deut. Med. Woch.* 1935. Mar. 1. Vol. 61. No. 9. pp. 332-336. [22 refs.]
- HENRY (A. F. X.). Flocculation mélanique et instabilité sérique. Courbes de malarieflocculation. Le clavier sérologique du paludéen.—*C. R. Soc. Biol.* 1935. Vol. 119. No. 21. pp. 597-600.
- KIKUTH (Walter). Die experimentelle Chemotherapie der Malaria.—*Deut. Med. Woch.* 1935. Apr. 12. Vol. 61. No. 15. pp. 573-577.
- KIKUTH (W.) & SCHÖNHÖFER (F.). Erwiderung auf vorstehende Arbeit von Kritschewski und Pines.—*Klin. Woch.* 1935. Jan. 5. Vol. 14. No. 1. p. 24.
- KRITSCHESKI (J. L.) & PINES (A. I.). Die Wirkung der Chinolinderivate auf Gametocyten von *Plasmodium praecox*. Eine Erwiderung auf den Artikel von W. Kikuth und W. Schönhöfer "Zur Frage der Gametocytenwirkung des Plasmodiums" in Jg. 1934, Nr. 24 dieser Wochenschrift.—*Klin. Woch.* 1935. Jan. 5. Vol. 14. No. 1. pp. 23-24.

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[This paper is the same as that noticed on p. 418 *ante*, with slightly different title.]

LINDBERG (K.). Notes on Malaria on the Barsi Light Railway (Deccan).—*Records of the Malaria Survey of India*. 1935. Mar. Vol. 5. No. 1. pp. 51-95. With 3 graphs. [10 refs.]

LIU (Lansing S.). The Prevalence of Malaria among Railroad Workers at the Hunan Kwantung Border.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 159-164. With 1 map. [12 refs.]

LIU (K. B.). Observations on the Treatment of Malaria with Atebrin, Malarcan, Totatquina, and Quino-Plasmoquine.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 299-302.

MESNARD (J.) & TOUMANOFF (C.). Contribution à l'étude des habitudes trophiques des anophélines de la Cochinchine.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 53-63. [10 refs.]

MITCHELL (Edward Clay) & GOLTMAN (David W.). Clinical Results in the Treatment of Malaria with Combinations of Quinine, Atabrine and Plasmochin during Four Years' Experience.—*Southern Med. Jl.* 1935. June. Vol. 28. No. 6. pp. 536-542.

MORIN (Henry G. S.). Sur l'activité prophylactique du service antipaludique des Instituts Pasteurs d'Indochine.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 107-128. With 4 figs., 1 map & 2 charts.

MORIN (Henry G. S.) & CARTON (P.). De l'influence des facteurs climatiques sur la répartition de l'endémic palustre en Indochine.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 145-158. With 1 chart.

MORISHITA (Kaoru). On *Anopheles (Myzomyia) indefinitus* (Ludlow, 1904) in Formosa. Adjustment of *A. formosensis* II, *A. rossii* and *A. vagus* Problem.—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa)*. 1935. May. Vol. 34. No. 5 (362). [In Japanese pp. 558-576. With 1 fig. [24 refs.] English summary pp. 577-578.]

MÜHLENS (P.). Are the Sequelae of Malaria contracted on Active Service Still Prevalent?—*Jl. Roy. Army Med. Corps*. 1935. Apr. Vol. 64. No. 4. pp. 247-249.

PRADO (Alcides) & GODINHO (Raul). Provavel caso autochtone de impaludismo registado en S. Paulo.—*Ann. Paulist. Med. e Cirurg.* 1935. Apr. Vol. 29. No. 4. pp. 295-297.

RAMOS (Jose). Algunas consideraciones referentes a la marcha del paludismo en San Fulgencio (Alicante).—*Rev. San. e Hig. Pública*. 1935. July. Vol. 10. No. 7. pp. 33-43. With 8 graphs.

ROBIN (L. A.). Observations sur la prémunition antipalustre chez l'Annamite adulte.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 129-144. With 3 graphs.

ROUKHADZE (N. P.). [The Deflection of *Anopheles maculipennis* by Domestic Animals and its Significance in the Prophylaxis of Malaria.]—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1-2. [In Russian pp. 121-125.]

RUSSELL (Paul F.) & BAIAS (Francisco). A Practical Illustrated Key to Larvae of Philippine Anopheles.—*Philippine Jl. Sci.* 1934. Dec. Vol. 55. No. 4. pp. 307-336. With 33 plates & 5 figs. [14 refs.]

SEREFETTIN (Osman). Atropische Cirrhose malarischen Ursprunges.—*Wien. Klin. Woch.* 1935. Apr. 12. Vol. 48. No. 15. pp. 466-468.

SHIPTON (Eva A.) & VICKERY (Donald). A Case of Congenital Malaria.—*Med. Jl. Australia*. 1935. May 25. 22nd Year. Vol. 1. No. 21. pp. 655-656.

- STEJSKAL (Karl). Kommen heute noch Kriegsmalariafolgen vor?—*Wien. Klin. Woch.* 1935. Apr. 26. Vol. 48. No. 17. p. 532.
- TILLEMA (S.). Malaria te Loa Koeloe. De lichamelijke weerstand als factor bij de malariabestrijding.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Apr. 2. Vol. 75. No. 7. pp. 574-576.
- TRENSZ (F.). Le rôle du système réticulo-endothélial dans le mécanisme de la séroflocculation palustre de Henry.—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 174-176.
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REVIEWS AND NOTICES.

CALCUTTA. **Twelfth Conference of Medical Research Workers held at Calcutta from 26th November to 1st December, 1934.**—pp. iii + 210. 1935. Simla : Govt. of India Press.

A congress of workers, in which those workers not only submit reports of progress but make an appeal to their fellows for their approval of the continuance of the work, has a special interest of its own. The business of the congress is, of course, not simply budgetary, for it affords an opportunity for workers to meet and discuss their researches. As in previous conferences the range of the subject matter is very wide ; it covers all those diseases, malaria, cholera, plague, rabies, leprosy, kala azar and others which have some title to be called the chief diseases of India, together with extremely interesting references to nutrition research, tuberculosis, the extent and intensity of extreme ultra-violet solar radiation, maternal mortality, yellow fever and cancer.

A new decision has been come to regarding the status of the Indian Research Fund Association which is now to be a local body *not* administered by the Government of India. This seems calculated to give even greater freedom to the medical control of the work done than hitherto. The conference although largely composed of government officials appears to have opportunity for fairly free speech, as is evidenced by the occasional incorporation of criticisms of government medical policy.

A series of 55 appendices contain for the most part the accounts of special research work. Cholera research is one of great importance. It is rather startling here to find an expression of doubt of the value of statistical analysis of figures for the effect of bacteriophage in the prevention of cholera. This however, presumably, is not a reflection on what is generally regarded as the only means available for dealing with the case of prophylaxis or treatment in the field but to the difficulty of obtaining reliable statistics. The committee on this subject, too, has evidently not been entirely satisfied with certain of the statistical data. One notes with satisfaction a preliminary, although rather disappointing, attempt to put the question of efficacy of bacteriophage to rigorous experimental animal test with the use of *Past. pestis* as the test bacterium. Statistical data should be obtainable in laboratory controlled trials even though the persistent and distant carriage of bacteriophage does prove a considerable difficulty. A very interesting study of "carrier" cholera vibrios is presented, which should yield results of considerable epidemiological and public health importance. It deals with such subjects as the virulence of and protection afforded by carrier vibrios and the serological differentiation of vibrios. In the case of plague vaccine research many points might be noticed if space allowed. Since the beginning of the year a change has been introduced in the preparation of Haffkine vaccine. The seed is now obtained from blood obtained from human cases, instead of, as formerly, by passage of cultures through Madras rats (non-immune house rats).

Mention is made in one of the later appendices of investigation into the possibility of utilizing the solar rays for bactericidal purposes. That subject has only been dealt with in India in a very restricted sense and might yield important results especially if it were conjoined

with the suggestion here made of the use of the sun's rays prophylactically and therapeutically. Another announcement which excites interest is that "work on anaemias of pregnancy will once again be taken up." These anaemias are not special to India but the material available for trial of therapeutic measures is evidently superabundant there. Quite recently discussion has arisen over the relative values of quinine, atebirin and plasmoquine in malaria. In British India just as in Netherlands India the monkey is available as a supremely useful test animal and we have in this report some reference to "experimental work with *Plasmodium knowlesi* infection in *Silenus rhesus*."

In conclusion of this very brief and inadequate summary we may refer to the survey of cancer in India and to the statements "that malignant disease is not uncommon in India" and, "that the incidence of cancer in India stands at a figure not far removed from its incidence in the West." Much important matter for consideration and digest should emerge from a thorough going study of cancer data in India, some of which is already presented here; explanations, for example, of why buccal cancer and skin cancer fall heavier on the male than the female and on the Muslim than the Hindu. The duration for which the betel quid is retained in the mouth and greater exposure to direct sunlight are mentioned as factors. W. F. Harvey.

CALCUTTA. Annual Report of the Calcutta School of Tropical Medicine and the Carmichael Hospital for Tropical Diseases 1934 [CHOPRA (R. N.), Officiating Director].—182 pp. With 4 charts & 4 plates. 1935. Alipore: Bengal Govt. Press.

The annual report of the Calcutta School of Tropical Medicine is one of those useful and interesting publications which to some extent serves the purpose of a year book on the subject. Its matter may not be quite co-extensive with the entire field but covers a considerable part of it and especially the part which deals with important current research. A survey of the whole work is presented by the Director of the School and this serves to focus one's attention on the worker, his work, the objects he has in view and the results which he has attained. It forms a most useful introduction to the more specialized sectional reports which follow. Constant reference is made to the Carmichael Hospital for Tropical Diseases, which is attached to the school definitely for teaching purposes. The ability to call up from a waiting list a series of illustrative cases throughout the session of the school must add enormously to the impressiveness of the teaching given and it is no wonder that the Superintendent of the Hospital is moved "again to draw the attention . . . of medical practitioners to the fact that the Carmichael Hospital for Tropical Diseases is *not* an emergency hospital."

An interesting commentary on the modern methods of identification of bacteria or of bacterial infection is afforded by the remark of the Professor of Bacteriology, when he says that "the old routine Widal reaction for enteric infections, when three antigens only were employed, has been discarded and has been replaced by a fuller method employing five suspensions for the detection of flagellar agglutinins as well as four antigens for the detection of somatic agglutinins." Under the implied heading of dysentery, or dysentery-like diseases, where the patients were suffering from vague abdominal symptoms only and very few from

acute bacillary dysentery, there is an interesting table of the species and frequency of the organisms isolated. Shiga and Flexner bacteria were isolated only once and 28 times respectively as compared with 167 and 100 for *Bact. pseudocarinatus* and *Bact. asiaticus*. The number of specimens (3,675) examined corresponded to 1,220 patients. Other striking numbers in this analysis were 0, 131, 52 and 100 for Sonne, *Bact. alkaligenes*, *Ps. pyocyanea* and "other non-lactose fermenters" respectively.

Cholera research continues vigorously, as it should, in the reputed home of Asiatic cholera. Cholera phages have reached the letter L in their progress down the alphabet and, in addition to these, 15 different groups of vibriophages have been separated out. It is a new announcement to find that "what is required in a disease like cholera is not only something like bacteriophage that will destroy the vibrio, but something that can neutralize the toxins and thus act directly on the cause of the lesions. This agent would be a potent cholera antitoxin and this, combined with bacteriophage, would constitute the ideal method of treatment of cholera." Again the searcher after scientific truth in the field of therapy is puzzled by the remark that "the value of bacteriophage, if any, is very limited in the treatment of cholera." It is interesting to note—especially in its bearing on the view, which seems to have been definitely rejected in Europe, that true cholera vibrios may undergo transmutation—that "during the decline of the epidemic and the inter-epidemic period cases of clinical cholera passing non-agglutinating vibrios are far more frequent than during the epidemic period."

One affection in India which has, perhaps, not received the attention that it deserves from the research worker is "hill diarrhoea." There seems some prospect, according to this report, of this omission being remedied. It may not really be an omission, when one looks back on the researches which have already been carried through. This may be seen from the remarks that: (1) "The malady is popularly known as 'hill diarrhoea' and in some instances the disease has received specific names such as 'Poonaitis' . . . , 'Simlitis' and so on" and (2) "The results obtained indicate that a great many of the bowel disturbances in Darjeeling are due to micro-organisms both bacillary and protozoal, well recognized as causative agents of dysentery."

Dengue is a disease of which much is known, but much still remains unknown. Its insect vector is now well established and it is a very important disease in the commercial life of Calcutta. Here we learn that, "The maximum peak of *Aedes aegypti* breeding is in July and August; and this corresponds to the maximum intensity of fresh infections with dengue (August and September). . . . This accounts for the devastating epidemics of dengue which so often sweep the city and cause enormous financial loss."

In amoebiasis research has been made into the value of carbarsone, an organic arsenic compound and it would seem to be as effective as emetine without the untoward toxic action of the latter. Its arsenic content would seem also to be beneficial to the general condition of the patient.

Monkeys, as subjects of malarial infection, are certain to lend themselves to the elucidation of many still unsettled problems in malaria. An important finding in this connexion is the discovery that the "Singapore" monkey (*Silenus irus*), a macaque, appears to be almost always infested with latent malaria of its own, whereas the "Bengal"

monkey (*S. rhesus*), also a macaque, "appears to be entirely free from any naturally acquired malaria of its own . . . but extremely susceptible to monkey malaria by inoculation."

So we might continue to make interesting quotations from the several special reports but considerations of space must limit us to two more only, from the report of the Professor of Pharmacology. Daboia and other snake venoms are now receiving attention for their therapeutic possibilities. Investigation has shown that Daboia venom has a marked tendency to produce thrombosis and gangrene at the site of the bite and death is due to secondary shock. . . . That the nervous centres are not much affected is shown by the fact that in decerebrated animals exactly the same results are produced. . . . The symptoms of shock in daboia poisoning are not due to reflex impulses but are due to the local dilatation of the capillaries of the splanchnic area.

The administration of opium dope to infants, which is not unknown in this country, is treated under the heading of "Drug Addiction Inquiry," although the addiction in this case must be entirely involuntary and, as such, somewhat of a contradiction in terms. "Habitual administration of opium to infants . . . has been prevalent in India for many centuries. . . . The custom . . . has greatly declined during the last two or three decades. . . . The main reason for administering the drug is economic, the drug being given to keep the children quiet so as to allow the mother to carry out her work, whether in the factory or the field, unhampered. . . . The drug is usually discontinued when the child attains the age of 2 to 3 years. . . . The dose varies from $\frac{1}{8}$ to 3 grains daily. . . . The drug affects the child's health adversely and hinders growth."

W. F. Harvey.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. Transactions of the Ninth Congress held in Nanking, China, October 2-8, 1934. [Edited by WU LIEN-TEH, Director, National Quarantine Service & C. Y. WU, Senior Medical Officer, National Quarantine Service.] —Volume I. pp. xiv + 790. Volume II. pp. x + 1,000. With numerous plates, charts & tables. 1935. Nanking: The National Health Administration. [£2 nett per set of two vols.]

These Transactions, occupying two volumes of 790 and 1,000 pages respectively, appear within six months of the close of the Congress and this in the Far East where we do not expect to find the hustle of the West. This is attributable to the energy of the Editors, Drs. Wu Lien-Teh and C. Y. Wu, and to the fact that no proofs were sent to the authors of papers. The scientific matter is arranged alphabetically by subjects, Vol. I comprising from Bacteriology to Leprosy and Vol. 2 from Malaria to Surgery. It is not necessary here to say anything about the contributions since they will be noticed in their appropriate places, but it may be noted that under malaria there are 20 papers, under helminthology 15, leprosy 12, plague and cholera 4 each, kala azar 4; there are nearly 200 in all.

It is of interest to note what Resolutions were passed, for these are an Index to those diseases or conditions which are either not yet fully elucidated or are inadequately controlled. One stresses "the urgent advisability of adopting practical measures for the rat-proofing of vessels" and calls attention to how far similar methods could be

employed to keep railway systems free from rat infestation, and to the need for study of rodents other than the rat as plague hosts.

A cholera Resolution demands further investigation of "carriers" in the Far East, statistically controlled tests of protection conferred by anticholera vaccine, studies of the relation between the cholera and allied vibrios, and more exact information about the epidemic and endemic areas of cholera in the Far East. The malaria Resolution is reproduced elsewhere.

The volumes close with an Index of Authors and Subjects and the editors and all concerned may be congratulated on the result of their labours.

A. G. B.

- i. BIBLIOGRAPHY OF HELMINTHOLOGY FOR THE YEAR 1933. (Compiled by A. WALTON from Titles selected by R. T. LEIPER.)—101 pp. 1935. July. St. Albans: Imperial Bureau of Agricultural Parasitology. [8s.]
- ii. STILES (C. W.) & BAKER (Clara Edith). **Key-Catalogue of Parasites Reported for Carnivora (Cats, Dogs, Bears, etc.) with their Possible Public Health Importance.**—*Nat. Inst. Health Bull. No. 163.* Wash. (Continuation of Hyg. Lab. Bull. Ser.). 1934. Dec. pp. ii+913-1223. 1935. Washington: U.S. Govt. Printing Office.

i. This issue of the Bibliography gives the titles of 1,367 helminthological papers from 471 journals and of 25 monographs, dissertations and books on helminthology traced by the Bureau as issued during 1933. A "Publisher's Note" in the form of a loose printed slip states that—"From 1934 (Vol. III) 'Helminthological Abstracts' will be published by the Imperial Bureau of Agricultural Parasitology. The 'Bibliography of Helminthology' will no longer be issued separately but will be combined with it under the title 'Helminthological Abstracts incorporating Bibliography of Helminthology'."

[As the first four parts of Vol. III of "Helminthological Abstracts" have already appeared under their original unexpanded title and the publisher's imprint of the Institute of Agricultural Parasitology, the change now announced must in some way be made to operate retrospectively. "Helminthological Abstracts" edited by Professor Leiper, first appeared in 1932 as a Supplement to the *Journal of Helminthology* published by the Institute of Agricultural Parasitology of the London School of Hygiene and Tropical Medicine. Volume I—the only volume so far completed—gives a résumé of the helminthological literature of 1932 and reviews 891 of 1,304 papers traced by the associated Imperial Bureau of Agricultural Parasitology for that year. Volumes II and III which are concerned with the literature of 1933 and 1934 respectively, still await the issue of their concluding parts and indexes. The first part of Vol. IV, dealing with the 1935 literature, is dated July and was issued in September, 1935. The object of each volume is to cover the literature published in a single year, but in practice many papers have remained unnoted either owing to inaccessibility or to their not being thought worthy of review in "Helminthological Abstracts." The incorporation of the Bibliography of Helminthology will enable the titles of papers which are not printed with the abstracts in the earlier parts to appear in the

final part for each year. The subscription price for the new publication will remain the same as that for "Helminthological Abstracts," viz., 30s. each volume.]

ii. The present Bulletin forms part 8 of the Host Catalogue of the well-known Index Catalogue of Medical and Veterinary Zoology compiled by Stiles and his co-workers, and deals with the literature relating to parasites reported for carnivora. It is based on the combined catalogue of the Divisions of Zoology of the Bureau of Animal Industry and of the National Institute of Health (formerly Hygienic Laboratory) at Washington, D.C. As a working reference index it will be of great assistance to parasitologists.

R. L. S.

BUREAU OF HYGIENE AND ~~TROPICAL DISEASES.~~

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 11.]

CHOLERA.

RUSSELL (A. J. H.). **Cholera in India.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 389–398.

CHUN (J. W. H.). **An Analysis of the Cholera Problem in China with Special Reference to Shanghai.**—*Ibid.* pp. 399–409.

POLLITZER (R.). **The Behaviour of Cholera and Cholera-like Vibrios towards Blood and Milk Media.**—*Ibid.* pp. 411–419.

YANG (Y. N.). **A Serological Study on Cholera Vibrios.**—*Ibid.* pp. 421–429.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. **TRANSACTIONS NINTH CONGRESS, NANKING, CHINA, 1934.** Vol. 1. pp. 431–450.
—**Round Table Discussion on Cholera** [RUSSELL (A. J. H.), Chairman.]

A representative international conference on cholera attended by men with experience of the disease and held in one of the countries which is periodically afflicted with outbreaks of the disease has international importance. All the present controversial matter received its share of attention and ranged over such subjects as epidemiology, prophylaxis, classification, the vaccine and bacteriophage. Only some of the points dealt with can be commented upon and especially those of the nature of conclusions or proposals. These seem to have been restrained, critical and cautious, and their tenor to have been the necessity for a fresh examination of the whole subject of cholera and the cholera vibrio on a controlled and statistical basis.

Epidemiology and Prophylaxis.—Of the climatic factors which might be considered as related to cholera rainfall was picked out for special notice. Rainfall was not accepted by Russell as having any direct effect on incidence. It merely distributes infection. Epidemic areas have a combination of high relative humidity and high temperature, while these are not essential in an endemic area. The endemic areas [or as we may call them the homes of cholera] are the great rivers of the East and especially their deltaic tracts. In India the decennium 1923–32 shows the lowest incidence of cholera on record and in seeking for causes for this result Russell makes mention of two possible factors, the extension of public health service and the distribution of bacteriophage, with the qualifying remark: "Future experience . . . will prove . . . whether these new factors have had the effect which enthusiasts may be inclined to claim on their behalf."

He abandons the tentative attitude implied in this statement, however, when he says of anti-cholera vaccine. "The statistics we

possess . . . prove conclusively that in this prophylactic . . . we have a valuable preventive weapon against cholera." It is also evident that he is an advocate, on statistical grounds, of the greater efficacy of bilivaccine *per os* over subcutaneous anti-cholera vaccine, and it is surprising to find that the "Office International" when referred to on this point "declared that while vaccination *per os* probably produces a certain immunity, this is much inferior to that obtained by subcutaneous inoculation." Other contributors to the subject of the epidemiology of cholera dealt to some extent with endemicity. Thus Chun says with some emphasis, "To our mind there is little doubt that cholera is endemic in the central Yangtze valley" and "The more we study the cholera problem the less tenable becomes the theory of an importation of the infection." [Such pronouncements should go some way towards dispelling the notion that Bengal is the home of cholera.]

Vibrio Classification.—Russell referred to the investigation of 4,000 vibrios freshly isolated in Calcutta from cholera cases, convalescents, carriers and from nature. "The main conclusion reached is that there is a very close relationship between the so-called 'authentic cholera vibrio' and the other vibrios." In the work of Pollitzer a further vibrio character—the curdling of milk—was added to those of haemodigestion and haemolysis for the purpose of grouping. He seems inclined to admit the possible existence of strains intermediate in character "between the ordinary water vibrios (which they resembled in blood and milk reactions) and the typical cholera vibrios (to which they belonged serologically)." Yang considered the subject of transformation and claims to have effected the transformation of non-agglutinable water vibrios into agglutinable vibrios by "daily transfers in sheep serum broth or broth."

Bacteriophage.—A communication by PANDIT dealt with the use of bacteriophage. His verdict may be very briefly expressed as follows: In treatment the evidence was that, administered within the first 24 hours of the disease a 50 per cent. reduction of mortality might be expected but that after 23 hours there was no reduction. The case for prophylactic value was stated as: (a) that it did not prevent the onset of infection but had an effect similar to that of administration curatively within 24 hours of the disease; and (b) that it reduced the number of secondary cases in a treated area.

Vaccine.—Russell who, as already stated, is in favour of the use of anti-cholera vaccine prophylactically also alludes to the different action of the particulate and fluid components of a vaccine. "The immunising value of cholera vaccines prepared (a) from bacterial deposit, (b) from the supernatant fluid, and (c) from a mixture of deposit and supernatant fluid has revealed that vaccines prepared from supernatant fluid are not only very toxic but possess little protective value. Those prepared from bacterial deposit are highly protective." [The reverse would appear to hold good of plague vaccine.]

Discussion.—In the round table discussion following the papers many delegates took part. The trend of the discussion is embodied in certain general resolutions. They were that: 1. Further investigation is desirable into the question of "carriers" of cholera and this should be carried out in the countries of the Far East. 2. Further statistically controlled field tests should be carried out of the protection conferred by anti-cholera vaccine especially in those countries where such tests have not yet been done. 3. Further study of the relationship

between the cholera vibrios and their variants is desirable. 4. Further field and statistical work should be carried out to obtain more exact information regarding the epidemic and endemic areas for cholera in the Far East. *W. F. Harvey.*

NICHOLLS (Lucius). **Carriers of *V. cholerae* who enter Ceylon from South India.**—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 713–744. With 2 maps & 3 graphs.

Much information regarding carriage of the cholera vibrio, the infectivity of the carrier, and the relation of non-agglutinable cholera-like vibrios to the true cholera vibrio may be derived from quarantine camps such as the well-known camp of Tor and that which is here in question at Mandapam in South India, especially if the data are taken in conjunction with developments after departure from quarantine. At Mandapam camp the stools of as many labourers and 3rd class passengers as possible are examined for *V. cholerae* and even though an agglutinable vibrio is found this does not mean any delay in continuation of the journey to Ceylon. All the vibrios isolated are placed in three groups which are compared with the cholera vibrio: I agglutinable, cholera-like; II non-agglutinable but cholera-like; and III non-agglutinable, morphologically and culturally unlike, vibrios. Samples of stools from 100,896 persons have been examined. Group I vibrios were isolated 84 times, Group II 2,838 times and Group III 992 times. We turn now to the records of cholera in Ceylon for 9 years 1925 to 1933. "Cholera has occurred on 30 occasions in the 9 years under consideration. On 21 occasions only one person was affected and the other 9 were outbreaks in which 3 or more persons acquired cholera." This is not a serious epidemiological history. On 10 occasions cholera occurred in the areas to which the estate labourers went and "on 9 of these occasions the disease was due to a recent arrival being in the incubation period." The nature of the journey to Ceylon was such as should have facilitated distribution of the cholera vibrio and therefore: "Since no case of cholera has occurred in Ceylon for the last ten years, in which it could be assumed that the patient had acquired the infection on the journey, it is strong evidence for the low virulence of the agglutinating vibrios of carriers." Nevertheless the author does not subscribe wholly to the view that only persons actually suffering from cholera and those in the incubation stage are infective. As regards seasonal prevalence and the relation of cholera-like to the cholera vibrios, it was found that during the cholera season in Madras Group II vibrios may occur in 10 per cent. of the estate labourers and that the prevalence of this group falls to 1 or 2 per cent. during the dry season. By "taking all the evidence into consideration it is difficult to avoid the conclusion that the vibrios of Group II are non-agglutinable avirulent *V. cholerae*." [See also *Trop. Dis. Bull.* 1934. Vol. 31. Suppl. p. 112*.] *W. F. H.*

DOORENBOS (W.). Note préliminaire sur la recherche des porteurs de vibrions au lazaret de Tor, chez les pèlerins retournant du Hedjaz. [**Vibrio Carriers at Tor in Pilgrims from the Hedjaz.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 268–272. With 1 fig.

The total number of examinations for vibrio carriers made at Tor since 1930 is 39,217. All the vibrios isolated have been minutely

examined in the laboratories of Tor and Alexandria, and their agglutination tested with various sera including a "standard" serum. It is obvious that the experience accumulated on such a large body of evidence must be of the greatest importance in connexion with the identification of the true cholera vibrio and the value of the measures adopted for control of spread of the disease. Agglutinating and non-agglutinating vibrios have been found at Tor but during the last five annual pilgrimages not a case of cholera has declared itself at this encampment.

The author enunciates his well-known views in this article, views which would gather within the fold of the true cholera vibrio the El Tor vibrio, paracholera vibrios, and others under the denomination of endemic disequibrated cholera vibrios of low virulence, causative only of sporadic cholera. The epidemic form of cholera is due to a contrasted type, the *Vibrio cholerae typus epidemicus* (see this *Bulletin*, ante, p. 457).
W. F. H.

BANERJEE (Dhirendra Nath) & DATTA (Sunil Krishna). **Cholera Kidney—a Histological Study.**—*Jl. Indian Med. Assoc.* 1935. June. Vol. 4. No. 10. pp. 441-444.

Twenty-six specimens of cholera kidney were examined and five of these were from patients dead of uraemia with total anuria for several days. A large range of special stains were used. The results were that: 1. With ordinary stains very little change could be detected in the glomeruli. 2. The glomeruli showed, with special staining, "thickening of the basement membrane with proliferation of both the epithelial and endothelial cells of the tuft." In many of the glomeruli focal necrosis, with hyaline change and sclerotic atrophy, was prominent. These were invariably present in all patients dying of uraemia. 3. Tubular changes were those of the epithelium of the convoluted tubules. Various casts were present in the tubules. 4. Interlobular vessels were always thickened in cases of uraemia.

W. F. H.

NARAYANA RAO (Y. S.). **A Plea for the Use of Concentrated Saline in Cholera.** [Correspondence.]—*Indian Med. Gaz.* 1935. May. Vol. 70. No. 5. pp. 296-297.

The question is asked by the author whether the advantage of administration of hypertonic salt solution in cholera may not lie more in the intravenous administration of salt than of the fluid in which it is dissolved. That this supposition has some foundation seemed to emerge from the treatment of four collapsed or collapsing cases of cholera with not more than 20 cc. of 20 per cent. salt solution and the revival of the circulation—as indicated by the passing of urine—within a few minutes after injection. At least the method might, on account of its simplicity, provide a first aid measure.

W. F. H.

MORISON (J.). **Bacteriophage in Cholera.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. 17. Vol. 28. No. 6. pp. 563-570.

Although in this communication Morison traverses well-known ground there is always matter of interest in the most recent expression

of views on the nature and mode of action of bacteriophage. At the present time eleven types of cholera bacteriophage have been isolated. This is an addition of two new ones to the former nine. Nor are the types wanting in distinctness. They "are as distinct from each other as species."

Perhaps one of the most interesting phenomena in connexion with the phage question is that which relates to the resistance or susceptibility of suitable cholera vibrios to phage action. Its importance lies in the way in which it is used for the analysis of phage types. "If we use a strain of cholera vibrio lysable by all our phages and grow it in tubes of broth each containing one of the types of phage, we get strains of cholera, each of which is resistant to one type of phage and is lysable by all the other types. Again, if we grow a susceptible cholera vibrio with all but one of these types, it becomes resistant to all but one of the phages." A series of communications have been appearing now for some time on the extraordinary effect of phage in causing transformation of the characters of an organism. In this connexion what we may call Morison's "511 experiment" is of great interest. "When cholera phage types were taken in combinations of two or more at a time the action of the combination was frequently different from the action of the individual components of the combination. This suggested an experiment in which the 511 possible combinations of our nine types of phage were tested on the same smooth *Vibrio cholerae*. The result was that we had changes in the morphology, the colonies on agar, the growth in broth, the salt stability, the agglutinability and the ability to ferment sugars which varied with the combination of types of bacteriophage and the period of action." These are remarkable changes especially if they are in any sense permanent and irreversible. Much of the main action of a phage, the solution of its corresponding bacterium, is ascribed to hydrolysis of the bacterial protein. Here also it is claimed that "no two types of phage exert the same enzyme action."

The second part of this informative article is occupied with the Nowgong-Habigunj field trials and it concludes with a reference to other bacteria awaiting the attentions of the worker with phages and phage types, "diseases like diphtheria, scarlet fever, streptococcal infections, coli infections, influenza and the typhoid group which show rises and falls in their virulence which have not yet been explained."

W. F. H.

WASSÉN (Anders). Essais d'application au vibron cholérique de la méthode fondée sur la faculté de déplacement des bactéries. [**Attempts to apply to the Cholera Vibrio Methods founded on Differential Separation of Bacteria.**—*Bull. Office Internat. d'Hyg. Publique*. 1935. June. Vol. 27. No. 6. pp. 1121-1134. With 2 figs. on 1 plate.

The methods referred to depend essentially on the motility of the organisms concerned and the use of filter paper saturated with an "H" specific agglutinating serum imbedded in a suitable semi-solid agar medium. Such a medium sown with artificially prepared test faecal material and incubated should give a differential outward movement of the specific bacteria, which will enable them to be collected and isolated for diagnosis. The method has proved, so far,

successful with paratyphoid organisms. In the case of the cholera vibrio very successful enrichment methods, using peptone water or alkaline blood are already known and employed. It remains to be seen what, in actual practice, this new technique can do. The medium used, containing usually 3 per cent. peptone (Parke Davis), 1 per cent. Liebig's extract, 0.3 per cent. sod. chloride and 0.35 per cent. agar, had a pH of 8.6. It is necessary to alkalinize it with sod. hydrate (1 cc. 10 per cent. per 100 cc. medium) and not sod. carbonate and to dilute it, if not of the right consistency, with 3 per cent. peptone bouillon. Other additions, intended to restrict the movement of organisms such as *Proteus vulgaris*, *Bact. coli* and *Ps. pyocyanea*, were: for 100 cc. medium 5 cc. 0.1 per cent. cadmium chloride and 5 cc. 1 per cent. pot. chlorate. The sod. hydrate and cadmium chloride must be mixed separately with the agar in order to avoid precipitation. An artificial stool containing, it might be, as few as 7 cholera vibrios, was introduced into the medium in amounts of 0.5 to 1 cc., at the side of the glass container by means of a pipette: care was taken to push the point of the pipette in various directions so as to lacerate the agar, and also to make the inoculation at a distance of a few millimetres from the wall. Strips of filter paper (5 × 20 mm.), saturated with specific serum (titre 1 : 25,000 and dilution 1 : 5), were inserted close to the inoculum and produced a characteristic agglutination of the advancing organisms, if these were specific. The appearances can be read off, after a variable time at 37°C., as positive or negative.

The author hopes that his method may result in the saving of an appreciable amount of time on the accredited methods for diagnosis of cholera.

W. F. H.

PHAM (H. C.). L'action de l'endotoxine cholérique sur le système neuro-végétatif abdominal. [**The Action of Cholera Endotoxin on the Abdominal Sympathetic System.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 16. pp. 78-80.

On the analogy of similar work with typho-paratyphoid endotoxin the author has injected small doses (0.05 to 0.1 cc.) of cholera endotoxin in the neighbourhood of the splanchnic nerve in guineapigs (460 gm.). The symptoms and lesions resembled those of cholera; similar results were obtained in the rabbit in doses of 0.2 cc. These symptoms were: dyspnoea, hypothermy, abdominal distension, and death in a few hours. With smaller doses the death of the animal was delayed for 3 or 4 days and it showed diarrhoea, oliguria, marked albuminuria and emaciation. Post-mortem there were found ecchymosis on the caecum, haemorrhagic infiltration of the terminal portion of the small intestine, congestion of Peyer's patches, desquamation of the mucosa the debris of which was found in the lumen of the intestine, vascular dilatation and haemorrhage, hyaline degeneration, oedema and haemorrhage in renal glomeruli, with some endothelial proliferation and cytolysis of tubular epithelium. Except for some diffuse parenchymatous hepatitis and suprarenal hyperaemia the other organs appeared normal. The doses used to produce these effects contrast markedly with the trivial effects produced by a subcutaneous injection of as much as 1 cc. endotoxin and with the lethal dose (about 0.8 cc.) by intra-cardiac injection.

W. F. H.

TAKANO (Shichiro). **Studies concerning Immunological Variability of Cholera Vibrio.**—*Kitasato Arch. Experim. Med.* 1935. Apr. Vol. 12. No. 2. pp. 101–138. [27 refs.] [Summary appears also in *Bulletin of Hygiene.*]

A large amount of work has been carried out on the mutation or transformation of cholera vibrios and much controversy has arisen as to the identity of various vibrios found in nature with these artificially transmuted cholera organisms. Most of the author's investigation deals with the variations which can be produced by growing the cholera vibrio in immune sera. Two types of known vibrio immune sera were used, the Inaba or normal type and the Takano or atypical serum. The corresponding strains were each cultivated in bouillon containing one or other of the immune sera, that is each in a homologous and a heterologous serum respectively. By repeated cultivation in these media four variant strains were obtained, all of them highly motile, giving opaque colonies on agar, the surfaces of which were rough dry and granular, and all spontaneously agglutinable. In other cultural respects the four strains differed from one another. Serologically the four variant strains were divisible into three types: No. 1 type "was obtained by culturing typical strains in an immune serum of the typical strain," with the result that it became difficult of agglutination by the immune serum of either a typical or atypical strain. No. 2 type emerged by cultivation of an atypical strain in an atypical, that is homologous, serum by which it became a typical strain; and No. 3 type was "obtained by culturing a typical strain in immune serum of an atypical strain." This last type was unchanged by the cultivation. It was further found that the characters acquired by these strains did not change by cultivation in ordinary agar media for as many as 150 generations.

W. F. H.

TAYLOR (J.) & AHUJA (M. L.). **Serological Relationships of Certain Vibrios Isolated from Non-Cholera Sources in India.**—*Indian J. Med. Res.* 1935. July. Vol. 23. No. 1. pp. 95–119. With 10 charts. [Summary appears also in *Bulletin of Hygiene.*]

The characters of the true cholera vibrio seem to be as far off settlement as ever. In this publication a minute investigation is carried out into serological characters of (1) vibrios isolated from healthy individuals in an endemic area, (a) agglutinable and (b) inagglutinable, and (2) a vibrio isolated from water in a non-endemic area which had been free from epidemic cholera for a prolonged period. For the investigation high titre sera and suitable suspensions of test organisms which were intended to bring out "O" and "H" agglutination were used. The sera were prepared with (a) living vibrios, (b) suspensions heated at 55°C. for 30 minutes and suspensions boiled in alcohol for 1 hour respectively while the testing suspensions were (a) living cultures, (b) formalinized cultures, and (c) cultures heated at 100°C. for 1 hour.

The results are summarized as follows: (1) Agglutinable vibrios isolated from healthy individuals in an endemic cholera area have been found to be serologically indistinguishable from an authentic vibrio strain maintained in subculture. (2) A vibrio isolated from water in an area widely removed from places where cholera is endemic and which had been free from cholera for a number of years was

inagglutinable when first received, but in a period of 6-months' subculture developed all the biological characters of an authentic cholera vibrio including "H" and "O" agglutination to full titre, and was indistinguishable from a cholera strain when quantitative and qualitative tests were applied. This strain differed in chemical structure from the cholera strain with which it was compared and from the agglutinable "carrier" vibrios. (3) Vibrios possessing five different types of chemical structure, as shown by the nature of their protein and carbohydrate fractions, have given identical serological and biochemical reactions. (4) A series of inagglutinable vibrios isolated from healthy individuals in the same endemic cholera area have not been found to fall into any consistent serological group. W. F. H.

LINTON (Richard W.); MITRA (B. N.); SEAL (S. C.); SHRIVASTAVA (D. L.). **Studies on the Antigenic Structure of *Vibrio cholerae*. Part VIII. The Specific Carbohydrate Content and Serology of the Acid-Soluble Fractions** [LINTON, MITRA & SEAL].—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 617–631. With 1 graph. **Part IX. Dissociation and Changes in Chemical Structure** [LINTON, SHRIVASTAVA & MITRA].—*Ibid.* pp. 633–657. With 3 figs. on 1 plate. [20 refs.]

Part VIII. A previous study [*ante*, p. 461] had reference to the three fractions "A," "B" and residue into which vibrios can be divided by extraction with acid alcohol. It has now been found that reducing substance (carbohydrate) "is present in both the fractions and in the residue and that the quantity in the latter is minute in proportion to the amount of the latter, which averages 85 per cent. of the whole vibrio. The 'A' and 'B' fractions have . . . proportionately large amounts of reducing substance." The "A" fraction probably represents the outer parts of the vibrio and shows high serological activity while "the 'B' and residue portions are almost inactive, although capable of giving rise to active, non-specific anti-sera. The anti-serum to the 'A' fraction is also non-specific." "A parallelism appears to exist between smoothness, as shown by . . . Millon's reagent, and the presence of more reducing substance in 'A' than in 'B' fraction."

Part IX. A series of 16 vibrios, chosen on the basis of their variability, are here studied with the idea of elucidating some of the chemical changes which underlie dissociation. The variation and dissociation in these vibrios is ascribable to at least three factors: (1) Loss of specific carbohydrate, which is probably the chief basis for the transition from a smooth to a rough development. (2) Change in constituents as exemplified by a vibrio giving rise to a daughter strain in which the protein and carbohydrate "are both different from those of the parent." This daughter, rough, strain had changed its protein to that which is characteristic of water vibrios and had developed an entirely different type of specific carbohydrate, consisting of glucose units alone, from the specific carbohydrates of types I and II, which are galactose and arabinose respectively. (3) The displacement of one chemical type by another. This phenomenon consisted of a swinging alteration from one type of carbohydrate to another, for example from glucose to galactose and back again. It is obvious how serological reactions must change with alteration of this sort. "An anti-serum prepared against the strain, when one member was

in the ascendancy, might not agglutinate the strain at all when, after a few weeks or months, the other member had gained the upper hand." The same phenomenon appears to be manifest when "medusa-head" rough colonies gradually disappear and then reappear.

The authors set forth their six groups (*Bulletin of Hygiene*, Vol. 10, p. 271) of vibrios based on the combinations of two types of protein with three types of specific carbohydrate.

Study of four El Tor strains, included in the 16 test vibrios, provided interesting results. "They have been found to form a chemically distinct group, although one that is closely related to both the cholera vibrios (through the specific carbohydrate) and to the water-vibrios (through the protein)." W. F. H.

GARDNER (A. D.) & VENKATRAMAN (K. V.). **The Antigens of the Cholera Group of Vibrios.**—*Jl. Hygiene*. 1935. May. Vol. 35. No. 2. pp. 262-282. [25 refs.]

The importance of this thorough-going re-examination of the cholera group question will be obvious to anyone who is working on the subject. Suspicion, it is said, had arisen that the agglutinating sera provided for diagnosis of the cholera vibrio were not sufficiently specific. If these sera contain antibody common to *V. cholerae* and related organisms, this would account for recent findings of an "incredibly high proportion of healthy carriers." It may also happen that supposedly single cultures giving rise to more than one "type" may in reality be mixed cultures. Important work which is being done at present on polysaccharide and protein components of vibrios is not yet final and complete, but affords a classification not quite in accord with serological classification.

Very clear indications are given of the technique used by the authors in their separation into groups of about 100 races of cholera and cholera-like vibrios from a variety of sources. For the serological differentiation the suspensions were of (1) H-O type, veal broth cultures, incubated 24 hours and killed with 0.2 per cent. formalin and 0.2 per cent. chloroform, and (2) O type, 24-hour agar cultures in salt solutions, placed in boiling water for 2 hours. The antisera also were of two kinds: (1) H-O sera made by injecting rabbits intravenously with the formalinized unheated suspensions; and (2) pure O sera made with the saline agar suspensions boiled for 2 hours. Absorption tests were done with either living or boiled suspensions. The biochemical reactions resulted in vibrios being described as typical, atypical or non-fermenting. By a "typical" vibrio the authors mean "producing acid without gas in glucose, mannite, maltose, saccharose; giving the cholera red reaction and not fermenting dulcitol." The "atypical" vibrio diverges somewhat from the typical but has a general similarity to it, while the "non-fermenting" vibrio is one which fails "to acidify any of the carbohydrates mentioned" and exhibits other differences. Under the heading "cholera group" vibrios "typical" and "atypical" vibrios are included, but "non-fermenting" are excluded. Antigenic stability under long cultivation is assumed with these exceptions: (1) that change from inagglutinability on isolation to agglutinability immediately after seems not uncommon; and (2) that the rough variation involving the loss of the smooth O antigens need only be considered when "sufficiently pronounced to be detectable in ordinary

cultures." Rough antigens have not been investigated except to confirm the fact that "rough forms, if motile, have the common H antigen and are deficient in specific O component."

Another subject which has not been fully investigated is the effect of the very numerous bacteriophages that act upon *V. cholerae*, but the work done gives the authors "no reason to suppose that transmutation of species occurs under bacteriophage action." Again they reject the theory as not proven that, "*V. cholerae* (typus epidemicus) is transformed by the bacteriophage at the end of epidemic outbreaks into a disequibrated form (typus endemicus) which has temporarily lost its epidemic potentialities and gained the power of haemolysis."

The results of cross agglutination reactions, in which O sera and unheated suspensions were used, give—with the addition of the characters biochemical similarity and possession of a common H antigen—the working scheme advocated by the authors for classification of their cholera group vibrios into subgroups, which they regard as entitled to the denomination species. The cholera group of vibrios in this scheme consists of: (a) an O subgroup I containing (1) non-haemolytic (goat cells) cholera vibrios of types original, variant and middle, and (2) haemolytic (goat cells) El Tor vibrios of types original and variant (? middle); and (b) O subgroups II, III, IV, V, VI and individual races (mostly haemolytic) which are paracholera, cholera-like and some El Tor vibrios. All the standard stock cholera vibrios received from various laboratories fell into subgroup I as did also most of the haemolytic vibrios called "El Tor." The other subgroups contained several vibrios and the residue was made up of single vibrios, each with a different specific O component.

Some important notes are given by the authors under the heading "heat-labile (H) antigen," such as that: (1) all their vibrios conforming to the cultural and biochemical standard of *V. cholerae* possessed a common H antigen; (2) absorption of an H-O serum with homologous O suspension removed all agglutinins for O suspensions of all species, leaving the common H agglutinin intact; (3) absorption of an H-O serum with an H-O suspension of a different O subgroup removed the H agglutinin for all species, leaving the O agglutinin intact; (4) the H component may possibly not be completely identical in all species; (5) those vibrios differing widely from the cholera group in biochemical characters did not show the common H antigen of the group.

Some consideration is paid to a non-specific antigen demonstrated by the action of O sera on boiled suspensions and it is indicated that the non-specific O reaction is explainable in one of two ways, either that the common flagellar (H) antigen is changed by heat into a new common antigen, or (2) the boiling destroys the H and brings out a common component, which has been inert in the unheated vibrio. The first hypothesis is ruled out. One final remark will attract attention: "The term 'agglutinable' in so far as it refers to the use of sera containing the non-specific H agglutinin must clearly be discontinued. All the official diagnostic sera hitherto in use have been of this type."

At the risk of making a long summary too long we add some of the authors' own conclusions: (1) The heat-stable antigens are divisible into: (a) a considerable number of specific antigens, best demonstrated by O sera and H-O suspensions, which serve as a basis of classification into O subgroups; and (b) a non-specific component

demonstrable with O sera and O suspensions. (2) The first subgroup contains all the standard cholera vibrios from central laboratories and is considered to be the only class of vibrios known for certain to cause epidemic cholera. (3) The haemolytic "El Tor" vibrios are serologically diverse and the term should be reserved for those with the same specific O component as the standard cholera vibrios. (4) For the identification of the undoubted cholera vibrios a standard subgroup I O-serum is recommended in conjunction with the haemolytic test and this should contain both the main and the subsidiary antigens of the subgroup. (5) As a working rule it is suggested that bacteriological proof of "cholera" or a cholera carrier should rest on the isolation of a non-haemolytic vibrio with the specific O antigen of subgroup I.

W. F. H.

SCHOLTENS (R. Th.). Analyse des récepteurs du vibron cholérique et du vibron El Tor. [**Cholera Vibrio and El Tor Receptors.**]—*Acta Leidensia (Scholae Med. Tropicae)*. 1934. Vol. 9. pp. 222–231. [Summary appears also in *Bulletin of Hygiene*.]

The subject matter of the author's analysis of cholera and El Tor vibrio receptors was extracted in this *Bulletin*, Vol. 31, p. 312. We may give here his conclusions: (1) Some sera agglutinating the cholera vibrio contain two agglutinins which are active to high titre. (2) One of these agglutinates all the vibrios and was called agglutinin A. The other agglutinates only a third of the vibrios and was called agglutinin B. (3) Both cause the same sort of flocculation. (4) Only those strains which are agglutinated by both agglutinins give rise to the two. (5) One strain although agglutinated by agglutinin B did not give rise to it on inoculation into the rabbit. (6) Both receptors are thermostable. (7) Both immunological types were found side by side. (8) Both immunological types were found among the so-called El Tor vibrios. In this respect the El Tor vibrios are identical with the cholera vibrios.

W. F. H.

VASSILIADIS (P. Ch.). Activité des hémolysines des vibrions cholériques et El Tor. [**Haemolysins of the Vibrios of Cholera and El Tor.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 18. pp. 332–334.
 —. Hémolysines des vibrions cholériques vrais. [**Haemolysins of the True Cholera Vibrio.**]—*Ibid.* pp. 339–341.

i. The author has already shown that the true, non-haemolytic cholera vibrios are transformed into haemolytic strains by culture in glucose media. Some further research has been made into this question of the influence of culture media on the production of haemolysins. It has been found that growth in liquid media and serial subculture stimulate the production of haemolysins.

ii. The evidence for haemolytic power may be indirect and given by the antihaemolysin produced by antigenic compounds of the various vibrios. Rabbits were injected with filtrates of vibrio cultures and the serum obtained was anti-haemolytic. Moreover it was discovered that the ordinary anti-cholera agglutinating serum of the laboratory neutralized the El Tor haemolysin at the same titre as the anti-haemolytic serum to El Tor vibrios.

W. F. H.

SCHOLTENS (R. Th.). Sur l'hémolyse du vibriion cholérique sous l'influence du bactériophage. [**Haemolysis of the Cholera Vibrio under the Influence of Bacteriophage.**—*C. R. Soc. Biol.* 1935. Vol. 119. No. 25. pp. 1023-1025.]

A secondary culture of the cholera vibrio on agar was used to inoculate (isolated colonies) 15 tubes of bouillon containing 0.5 cc. sheep blood. These cultures all showed growth on the following day. Those of flocculent growth gave a slight but definite haemolysis while the haemolysis with those of diffuse growth was almost negligible. Haemolytic cultures proved to be resistant and non-lysogenic.

W. F. H.

LINTON (Richard W.), SINGH (Harwant) & SEAL (S. C.). **A Study of Vibrio Filtrates.**—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 659-674. With 1 plate.

Schwartzman's phenomenon on which this study is concentrated is possibly anaphylactic. He made intracutaneous injection into a rabbit of 0.25 cc. of a filtrate of a young culture. This gave practically no reaction, but if it was followed by intravenous injection in 24 hours of 1 to 1.5 cc. of filtrate a severe and haemorrhagic reaction with necrosis appeared at the site of the former injection. The same occurs with filtrates of 20-hour agar cultures of vibrios. Of the fractions into which vibrios can be divided by extraction with acid alcohol "the 'A' fraction alone yields a constant and typical reaction" while "the whole vibrios and the 'B' and residue fractions are without sensitizing effect."

W. F. H.

BANERJEE (Dhirendra Nath) & DATTA (Sunil Krisna). Cholera Kidney. A Clinical, Biochemical and Functional Study.—*Jl. Indian Med. Assoc.* 1935. July. Vol. 4. No. 11. pp. 497-498.

LINTON (Richard W.). Une base chimique pour la classification et l'étude des variations des vibriions.—*Bull. Office Internat. d'Hyg. Publique* 1935. June. Vol. 27. No. 6. pp. 1108-1120.

LINTON (Richard W.) & SEAL (S. C.). The Effect of the Use of Living or Dead Suspensions of Vibrios on the Agglutination Titre.—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 68-70.

MANAKO (K.). Cholera and Cholera-like Vibrio. Parts IV & V. Variability of Cholera Vibrio.—*Jl. Oriental Med.* 1935. May. Vol. 22. No. 5. [In Japanese. English summaries pp. 79-80.]

MANAKO (K.). Cholera and Cholera-like Vibrio. Parts VI, VII and VIII. Variability of Cholera Vibrio.—*Jl. Oriental Med.* 1935. June. Vol. 22. No. 6. [In Japanese pp. 949-962. [11 refs.]; 963-975. [20 refs.]; 977-983. With 7 figs. on 2 plates; English summaries pp. 85; 86; 87.]

POLLITZER (R.). A Further Note upon Cholera and Related Vibrios in Shanghai Waters.—*Reports National Quarantine Service.* Shanghai, China. 1934. Ser. 5. pp. 61-69. With 2 graphs.

REPORTS NATIONAL QUARANTINE SERVICE. Shanghai, China. 1934. Ser. 5. pp. 185-220. With 1 chart.—Central Cholera Bureau in 1934.

VASSILIADIS (Pierre). Behavior of Cholera and El Tor Vibrios towards the Schwartzman Phenomenon.—*Jl. Infect. Dis.* 1935. July-Aug. Vol. 57. No. 1. pp. 118-120.

AMOEBIASIS AND DYSENTERY.

AMOEBIASIS.

SPECTOR (Bertha Kaplan), FOSTER (John W.) & GLOVER (Nelson G.).
Endamoeba histolytica in Washings from the Hands and Finger
 Nails of Infected Persons.—*Public Health Rep.* 1935. Feb. 8.
 Vol. 50. No. 6. pp. 163–165.

Seventy-four carriers of *E. histolytica* cysts were examined. Hands, débris under finger nails, and nail parings, were examined after defaecation and before hands were washed. Only 5 gave positive findings; 2 showed very few live *E. histolytica* large cysts; 1 showed very few dead *E. histolytica* large cysts; and 2 showed live small cysts. One man, a plasterer, showed a number of large cysts of free living amoebae.

Of these 74 washings 54 were cultured for *B. coli-aerogenes*, of which 15 were positive. These findings suggest that contamination of food by carriers of *E. histolytica* under the ordinary conditions of food handling rarely happens.

H. M. Hanschell.

ISKANDAR (Fayek). **Post-Dysenteric Oedema in Children.**—*Jl. Egyptian Med. Assoc.* 1935. Feb. Vol. 18. No. 2. pp. 134–137. With 1 chart.

Post-dysenteric oedema in children is accompanied by a definite fall in blood proteins.

The rôle played by plasma proteins in maintaining the colloid osmotic pressure of the blood and preventing retention of fluid in the interstitial tissues is well known.

Ten children suffering from post-dysenteric oedema were selected, after thorough examination had excluded nephritis or pyelitis. Their blood proteins, and those of 10 healthy control children of about the same age, were estimated by the Kjeldahl method. Serum was used instead of plasma because the fibrinogen fragment in plasma proteins is small (0.3 gm. per cent.) and appears to play no part in maintaining fluid balance between blood and tissues; and, moreover, the oxalate added to the tube in which blood for plasma is collected causes plasma to dilute itself by abstracting water from the cells and thus may significantly reduce the plasma protein concentration. These estimations made it clear that the post-dysenteric oedema was accompanied by a definite fall in blood proteins. On treatment (high protein diet) disappearance of oedema was accompanied by simultaneous rise in blood proteins. Increased capillary permeability as a factor in this oedema cannot be excluded.

H. M. H.

BONNE (C.). Over niet herkende amoebendysenterie bij lijders aan andere ziekten. [**Want of Recognition of Amoebic Dysentery in Other Diseases.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. Mar. 19. Vol. 75. No. 6. pp. 470–479.

A study of a dozen post-mortem reports from a first-class hospital revealed that the patients had died from some very serious illness

without recognition of the fact that they were at the same time suffering from amoebic ulceration. Further study of such cases has suggested to the author that amoebic dysentery, itself a serious disease, is not infrequently missed under such circumstances as the above and may itself be the actual cause of death. It may not have been possible to demonstrate the presence of amoebae in the stools during life. Examples of the types of serious disease in which this amoebic complication was found after death were:—aneurysm of the aorta and phthisis, cirrhosis of the liver, bronchiectasis and stone in the bladder, cancer of the uterus with metastases and vesico-vaginal fistula, gangrene of the foot with bronchopneumonia and ankylostomiasis, typhoid fever. It is a fact that, in the tropics, amoebiasis is not examined for as a routine practice and this ought to be done. The case is otherwise with respect to malaria, which no physician in the tropics is likely to ignore as a possible complication. In hospitals, too, the ritual of taking temperatures is strictly performed, but not the duty of recording the number of stools. The patient, moreover, may not be confined to bed and the record of this important symptom may have to depend on his own statement: constipation even may be the symptom and not diarrhoea. The material again which is chosen for microscopic examination may not be well chosen: it should be, if possible, a fragment of blood-stained mucus. Lastly the laboratory report when received may be negative, even when amoebae are present, for the technique of examination is delicate and may fail. The author is well aware that dysentery amoebae may be found in persons who have [apparently] a completely sound intestine and again that they may not be found even where the amoebic ulcers reach almost to the anus.

It is strongly advised that the physician in the tropics should be on the look out for amoebiasis just as he is always on the look out for malaria.

W. F. Harvey.

ESPOSITO (Giuseppe). Un caso non comune di amebiasi a localizzazioni multiple. [**An Unusual Case of Multiple Amoebiasis.**]—*Giorn. Ital. di Malat. Esot. e Trop.* 1935. July 31. Vol. 8. No. 7. pp. 170, 173–176, 179–181. With 3 figs.

The patient, a man of 35 years, gave a history that 14 months before coming under observation he had had an attack of diarrhoea with tenesmus and passage of blood and mucus for 3 weeks. This cleared up and for some months he was apparently well, returned to work and ate his customary food. Then there supervened an attack of fever with pain over the liver and later pain in the right side of the chest with cough and signs of bronchitis, and expectoration wine-coloured and streaked with blood. The liver area was swollen, dyspnoea very marked and X-ray revealed opacity of the right side of the thorax and upper part of the abdomen. Repeated exploratory puncture brought away 500 cc. or more of reddish-brown fluid. Emetine was given, later stovarsol and finally another course of emetine and the patient left hospital well, 40 days after admission. The diagnosis appears to have been made on clinical grounds and the result of treatment, for except for "some doubtful amoebae in cystic form" in the sputum on his arrival at hospital, amoebae were never found and experimental injection of kittens *per rectum* with the fluids extracted by puncture of the pleura and the liver proved negative. [The title of the paper therefore rather begs the question.]

H. H. S.

WU (T. T.) & CHI (C. K.). **Amoebiasis of Uterine Cervix. Report of a Case.**—*Chinese Med. Jl.* 1935. Jan. Vol. 49. No. 1. pp. 69–73. With 2 plates. [14 refs.]

The amoebae in this case were found in sections of cervical necrotic tissue obtained by biopsy. The amoebiasis of cervix was probably preceded by chronic cervicitis. Mode of infection uncertain; no history of dysentery; no rectovaginal fistula; no stool examinations.

H. M. H.

AKASHI (Kazuyoshi). **The Treatment of Amoebiasis with Iodochlorhydroxyquinoline.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa).* 1934. Dec. Vol. 33. No. 12 (357). [In Japanese pp. 1801–1806. English summary p. 156.]

The author treated 15 cases of acute amoebic dysentery and 5 *histolytica* cyst carriers with vioform with uniform success.

It was given by mouth, in tablet or powder, 0.75 gm. daily for 15 days. The dysentery cases were well in a week and no relapse has occurred in a period of 1–5 months. All the carriers also were cured after three days of treatment.

A. G. B.

MILLISCHER (P.). Essai de traitement de l'amibiase intestinale par l'acide iodo-oxyquinoléine sulfonique. [**Treatment of Amoebic Dysentery by Mixiod.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 99–103.

The report is favourable.

The author states that he has had first hand and satisfactory experience of emetine and stovarsol therapy in over 2,000 cases of amoebiasis; and it is with that partisan bias that he approached the trial of Mixiod (acide iodo-quinoléine-sulfonique) in amoebic dysentery. Observations on 22 cases lead him to conclude that Mixiod is most effective when given simultaneously by mouth and as rectal lavage. As compared with emetine its action is more definite and rapid on cyst carriers than on infections with trophozoites. In the latter Mixiod may entirely replace emetine where the latter is contraindicated although its action is slower and treatment must be more prolonged. Emetine dosage may be reduced if given with Mixiod.

H. M. H.

AKASHI (Kazuyoshi). **The Treatment of Amoebiasis with Gavano.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa).* 1935. Feb. Vol. 34. No. 2 (359). [In Japanese pp. 189–194. English summary p. 194.]

Ten cases of acute amoebic dysentery were treated with gavano, which proved "remarkably effective"; in the case of 3 carriers progress was slow.

The drug was given by mouth, and by injection in two cases. In the dysenteries after 2–3 days the number of motions was reduced and pain disappeared. After 3–4 days *E. histolytica* could not be found. No relapse occurred in 3–6 months. In the carriers cysts disappeared on the 7th, 8th and 9th days. There was no evidence of toxicity. Gavano is said to be a derivative of ipecacuanha [see this *Bulletin*, Vol. 31, pp. 282 and 652].

A. G. B.

AGRIKOLANSKI (N.) & TIBURSKAYA (N.). **On the Treatment of Amebiasis with Osarsol.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1935. Vol. 4. No. 1-2. [In Russian pp. 16-18. English summary p. 18.]

The authors report the results of treatment of 15 cases of amoebic dysentery with "Osarsol" (=Stovarsol=Spiroicide). The drug was administered three times a day in the course of four days, the doses being 1+1+2 tablets (0.25 gm. each) on the first two days, and 2+2+2 on the last two days (=20 tablets or 5 gm. "Osarsol"). The patients underwent 5-6 such courses with intervals of 6-7 days between them, with the result that a complete cure was effected in 11 cases. In two cases the treatment failed to expel the amoebae, while two others relapsed.

C. A. Hoare.

AFRICA (Candido M.) & GARCIA (Eusebio Y.). **Iodaseptine Cortial (Iodobenzomethylformine) in the Treatment of Chronic Amebiasis.**—*Jl. Philippine Islands Med. Assoc.* 1935. June. Vol. 15. No. 6. pp. 305-311. [12 refs.]

Symptoms, and cysts and trophozoites, disappeared in five cases of treated chronic amoebiasis after intramuscular injection of iodaseptine cortial. All had been subjected to other forms of treatment without success.

Iodaseptine cortial, or Iodobenzomethylformine, is a French patented preparation primarily designed for the treatment of pulmonary tuberculosis and chronic rheumatism. The five cases are described. There were no special dysenteric symptoms, only chronic diarrhoea alternating with constipation and pain and with loss of weight and strength. In every case cysts were found but trophozoites in one only. After "two series" or a few injections of the drug the symptoms disappeared and did not recur. In one instance cysts were absent three years later, in another 12 months. The authors suggest that a further trial is justified.

A. G. B.

NOSSINA (V.). **Action of Drugs upon *Entamoeba histolytica* in vitro.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 6. [In Russian pp. 451-459.]

The author studied the effect of emetine and yatren upon the dysentery amoeba cultivated in a fluid medium (John's combined with Barrett and Smith's media). Emetine has a slight action in an acid medium but the effect increases as the reaction approaches neutrality. At pH above 6.8 emetine kills the amoebae in a dilution of 1 : 5,000,000. Further rise in alkalinity does not increase the effect of the drug. The effective range of yatren is between pH 5.6-7.8 in a concentration of 1 : 5,000.

C. A. Hoare.

BERETERVIDE (Juan Jose) & GRAU (Carlos A.). **Una nueva sal de emetina : el canfosulfonato de emetina. [The Camphosulphonate, a New Salt of Emetine.]**—*Prensa Méd. Argentina.* 1935. Apr. 3. Vol. 22. No. 14. pp. 671-681. With 12 figs. [12 refs.]

The authors claim for the camphosulphonate of emetine the advantages that the depressing action of the base, emetine, is counteracted by

the acid radicle ; that experiments carried out with frogs, rats, rabbits, guineapigs, cats and dogs have shown it to be only one-third as toxic as the hydrochloride ; that clinically patients show greater tolerance for the new compound than for the older ; and, finally, that it should replace the older.

The authors give an account of the preparation of Reychler's camphor-B-sulphonic acid ($C_{10}H_{15}O.SO_3H$)₂, and of the emetine base and lastly of the compound. In testing the new drug, they find that the toxic action is due to the contained emetine and that it is a cardiac and central nervous system poison, and that, as stated above, the toxicity is only one-third of emetine hydrochloride. The dose employed in human subjects was 6 cgm. daily injected till 1.2 gm. had been given, *i.e.*, the course lasts for 20 days.

The two cases reported in detail are not very convincing of its efficacy. Both were cases of liver abscess with chocolate-coloured pus [but faecal examination in each case was negative for Entamoeba and none is mentioned as being found in the discharge]. Both were operated upon and in spite of injection of the new salt into the abscess cavity and of courses of it till the total mentioned, 1.2 gm., had been administered, in each case the abscess re-formed and more pus was removed at the second operation than at the first. To each patient three series of the injections were given before the condition cleared up. They were under treatment for 5 and 8 months respectively. [Since 6 cgm. is the usual dose of the hydrochloride, perhaps better and more rapid results might have been obtained with larger doses of the new compound since its toxicity was only one-third that of the hydrochloride.]

H. H. S.

FAUST (Ernest Carroll), SCOTT (L. C.) & SWARTZWELDER (J. C.).
Influence of Certain Foodstuffs on Lesions of *Endamoeba histolytica* Infection.—*Proc. Soc. Experim. Biol. & Med.* 1934. Dec. Vol. 32. No. 3. pp. 540-542.

KAGY and Faust 1930, and Faust and KAGY 1934, showed that raw liver and liver extract were distinctly beneficial to dogs suffering from acute amoebic enteritis and ventriculin consistently harmful to them [*ante*, pp. 190 and 191]. Faust discovered that dogs resistant to amoebic infection on a balanced diet could usually be infected if fed on canned salmon.

In the present experiments, 26 healthy young dogs were inoculated intracaecally (Faust 1931) with the same human strain of *Endamoeba histolytica*. All suffered from acute amoebiasis of a few days' standing when the tests were made. Fresh pigs' liver, ventriculin (Parke Davis & Co.) and commercial canned pink salmon (grade B) were the foodstuffs employed. One dog died, the other 25 were sacrificed.

Liver: 150 gm. unchopped raw liver fed to one dog daily ; clinical improvement ninth day : killed 13 days later, only few small shallow amoebic lesions in caecum and rectum. 60 gm. finely chopped liver in liver juice produced clinical improvement on 5th day ; killed 3 days later, only few shallow lesions in rectum. When only 12 gm. liquid and solid fractions of finely chopped liver had been introduced into large intestine of 3 dogs, 2 showed improvement on 4th day, one failed to improve ; autopsy revealed only few lesions in rectum of one dog ; numerous shallow lesions in large intestine of the other two. 60 gm. liquid and solid fractions of finely chopped liver given intracaecally daily procured marked improvement on third day ; and on sacrifice 2 days later only a very few pinpoint

lesions were found. Finely chopped liver autoclaved at 17 pounds pressure for 20 minutes and 60 gm. given daily orally (2) and intracaecally (2); all 4 dogs became rapidly worse; sacrificed on eighth day; multiple lesions throughout large intestine, many motile amoebae in lumen and in lesions. Chopped liver heated to 70°C. for 30 minutes to coagulate proteins; solid fraction doubly filtered and washed, fed orally, 85 gm. daily, to each of 2 dogs; liquid fraction (250 cc. solution from 100 gm. raw liver) given orally to each of 2 dogs; all 4 sacrificed on 22nd day. Solid fraction fed dogs revealed numerous deep undermining lesions, no healing; liquid fraction fed dogs revealed only very few small shallow lesions with extensive healing.

Ventriculin: 10 gm. suspended in 100 cc. water was given daily, orally to one dog, and intracaecally to 2 dogs; in all 3 infection became rapidly fulminating; on sacrifice, 2 on 9th day, one on 12th day, multiple deep lesions throughout large intestine in each, and in one a general inflammatory condition. *Ventriculin* 6 gm. in 50 cc. water, autoclaved (17 pounds pressure, 20 minutes), given daily orally to 2 dogs, intracaecally to 2; in all four improvement occurred and on sacrifice on 9th day relatively few active lesions were found.

Salmon, unaltered canned, was used routinely to exacerbate mild, chronic, or inactive infections. When macerated and given intracaecally the dog noticeably improved; on return to oral administration infection promptly fulminated. Peptic and tryptic digests of salmon given intracaecally daily (30 cc. containing 25 gm. canned salmon) caused rapid fulmination of infection; sacrifice on 10th day revealed large intestines studded with amoebic lesions.

Liver and ventriculin (15 gm. each suspended in 100 cc. of water daily); and liver and salmon (15 gm. each daily) were combined and given intracaecally. In the former experiment the liver failed to counteract effect of ventriculin; but in the latter marked clinical improvement and recovery were effected; and on sacrifice on 12th day, no amoebae and no unhealed lesions were discovered.

H. M. H.

DESCHIENS (R.). Modification de l'aptitude pathogène, pour le chat, de l'amibe dysentérique en culture. [**Change in Pathogenicity for the Cat of Cultures of the Amoeba of Dysentery.**—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 119-126.]

Eight strains of amoebae (all to start with haematophagous) have been studied—3 strains from France (autochthonous), 3 Moroccan, one Indo-China, one Madagascar—for pathogenicity to cats.

The strains were cultured in a medium containing rice starch, and the cultures maintained from three to eleven months. From two to four kittens were inoculated with each of the strains in culture. Of these 8 strains, originally virulent, 6 appeared to have lost their pathogenicity for the kitten, after culture in presence of rice starch; 2 maintained their pathogenicity, for which the duration of culture might account, as the 2 had been in cultivation less than three months, and the 6 for more than three months.

The author states that profound modification of the initial intestinal flora associated with the dysenteric amoeba, fermentation of the rice starch forming butyric, lactic, and propionic acids, acid reaction of the culture medium, could explain decrease or loss of pathogenicity if it be admitted that a proper flora associated with the amoeba is necessary to provoke amoebic dysentery.

[It is to be noted how few were the kittens inoculated with each strain.]

H. M. H.

MELENEY (Henry E.) & FRYE (William W.). *Studies of Endamoeba histolytica and Other Intestinal Protozoa in Tennessee: IX. Further Observations on the Pathogenicity of Certain Strains of E. histolytica for Kittens.*—*Amer. Jl. Hyg.* 1935. Mar. Vol. 21. No. 2. pp. 422-437. With 2 figs. [31 refs.]

The four strains of *E. histolytica* studied were maintained for nearly three years in culture on egg-Ringer medium, overlaid with horse serum-Ringer, and enriched with rice flour. The strains were tested at intervals during this period to determine pathogenicity for kittens. Similar experiments were made with seven other strains of *E. histolytica*. Twenty or more kittens were used in nearly all the series of experiments with each strain.

"In these series of experiments there was considerable variation in the percentage of kittens which became infected with each strain, but the average extent and intensity of the lesions remained fairly constant in all the series performed with each individual strain.

"The average degree of pathology produced by the two strains from the hill country of Middle Tennessee continued to be much less than that produced by the two strains from the bottom-land of West Tennessee.

"Experiments with seven other strains of *E. histolytica* are reported in which one series of twenty or more kittens was inoculated with each strain: one strain from a symptomless 'carrier' in Nashville showed a very low degree of pathogenicity. Two other strains showed an intermediate degree of pathogenicity. Four strains from Chicago all showed very high degrees of pathogenicity.

"These results corroborate our previous conclusion that it is possible to demonstrate by large-scale kitten experiments performed under uniform conditions that strains of *E. histolytica* of varying degrees of pathogenicity exist.

"The work has also demonstrated that some strains of *E. histolytica* maintain a constant degree of pathogenicity throughout a period of at least 3 years in artificial cultivation.

"Since even the least pathogenic strains which we have encountered produce lesions in some kittens, and since human beings may harbor potentially virulent strains without showing clinical symptoms, it is important that every person encountered in medical practice who is found to harbor *E. histolytica* should be treated with an amoebicidal drug."

H. M. H.

FRYE (William W.) & MELENEY (Henry E.). *Studies of Endamoeba histolytica and Other Intestinal Protozoa in Tennessee: VIII. Observations on the Intestinal Protozoa of Young Pigs and Attempts to produce Infection with a Human Strain of E. histolytica.*—*Amer. Jl. Hyg.* 1934. Sept. Vol. 20. No. 2. pp. 404-414. With 9 figs. on 1 plate. [11 refs.]

Ten young pigs were studied with reference to their natural intestinal protozoa.

Uninucleate amoebic cysts, 5 to 12 micra, were found in all. The authors describe them as having the combined characteristics of *E. polecki* and *E. deblickei*. Other natural intestinal protozoa found were Iodamoeba, Trichomonas, Chilomastix, Giardia, Balantidium, and a coccidium. Infections with Balantidium were eliminated by a single dose of heptylresorcinol (dihydranol). Carbarosone treatment permanently eliminated the *polecki-deblickei* amoebae from all of the pigs. Iodamoeba later reappeared in three pigs and Trichomonas in eight

pigs. All attempts to infect the pigs with a pathogenic strain of *E. histolytica*, either by direct injection into the ileum or by rectal injections failed, whether the pigs were on a normal diet, or on a high carbohydrate diet.

H. M. H.

PAVLOFF (P.). Recherches sur la présence de kystes à quatre noyaux d'amibes dysentériques dans les excréments des porcelets. [**Four-nucleated Cysts of *E. histolytica* in the Excreta of Pigs.**]—*Ann. Parasit. Humaine et Comparée*. 1935. Mar. 1. Vol. 13. No. 2. pp. 155–160. [12 refs.]

It was announced by KESSEL that pigs in China harboured amoebae producing cysts with four nuclei and that these injected into kittens behaved like *Entamoeba histolytica*. An examination of a large number of pigs in France and Bulgaria has not revealed any such infection. Uninucleated cysts similar to those described by PROWAZEK, CAUCHEMEZ and others occur.

C. M. Wenyon.

TANABE (Misao). **The Excystation and Metacystic Development of *Entamoeba histolytica* in the Intestine of White Rats.**—*Keijo Jl. Med.* 1934. Dec. 31. Vol. 5. No. 4. pp. 238–253. With 1 text fig. & 38 figs. on 3 plates. [12 refs.]

By feeding cysts of *Entamoeba histolytica* to white rats and making preparations from the intestinal contents at varying intervals the author has been able to follow the excystation process and the subsequent development of the excysted quadrinucleate amoeba. The findings agree in all essential respects with those obtained by DOBELL on cultures of this amoeba, which appears to be truly pathogenic to white rats. Three excellently executed plates containing 38 figures illustrate the author's findings.

C. M. W.

GNEZDILOV (V.). Contribution à la biométrie et à la statistique des kystes d'*Entamoeba histolytica* e d'*Entamoeba hartmanni*. [**Biometrical and Statistical Study of the Cysts of *E. histolytica* and *E. hartmanni*.**]—*Rev. Microbiol., Epidémiol. & Parasit.* 1934. Vol. 13. No. 2. [In Russian pp. 137–148. With 4 figs. [31 refs.] French summary pp. 148–149.]

The author made a biometrical study, using statistical methods, of over 2,300 cysts of the dysentery amoeba from three human carriers. He arrives at the conclusion that there exist two groups of amoebae differing markedly in the dimensions of their cysts: the one with large cysts belongs to *E. histolytica* (or *E. dispar*), the other with small cysts belongs to *E. hartmanni*. Each group contains a number of strains or races characterized by different average dimensions of the cysts, viz., those measuring on the average 6.93μ , 7.2μ , 7.75μ , 7.99μ and 8.25μ represent the group with small cysts, while those measuring 11.66μ , 12.85μ , 13.25μ and 14.47μ represent the one with large cysts. The specific status of the rare cysts with intermediate dimensions (9 – 11μ) requires further elucidation. It is suggested that since the biological properties of *E. hartmanni* are unknown, forms with small cysts should be treated separately in all works dealing with the incidence of the dysentery amoebae.

C. A. Hoare.

ZERTCHANINOV (L.). Sur la différenciation des kystes semblables à celles de l'*Entamoeba histolytica*. [**Differential Diagnosis of Histolytica-like Cysts.**—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 3. [In Russian pp. 267–273. With 4 figs. French summary p. 272.]

In the course of a coprological examination of the population in the Ural Region the author found that all the amoebic cysts of the *histolytica* type were of the small or medium varieties, measuring from 5 to 12 μ in diameter. In view of this fact, and because all the cases observed in this region were symptomless carriers, the author concludes that the infections are due to *Entamoeba hartmanni* and *E. dispar*, and not to *E. histolytica*. Apart from size he claims to be able to distinguish the first two forms from *E. histolytica* by the morphology of the vegetative or active stages and by the dimensions and amount of the chromatoid bodies. With a view to differentiating between *E. hartmanni* and *E. dispar* an examination was made of 5,136 cysts obtained from 25 cases, using statistical methods. The cysts were found to fall into two groups, those of the first, which are referred to *E. hartmanni*, have a diameter from 4.25 to 9.35 μ (average 7 μ) with chromatoid bodies in 75.5 per cent., while the cysts of the second group, referred to *E. dispar*, range from 7.5 to 14.45 μ in diameter (average 10 μ), and have chromatoid bodies in 40.6 per cent. of specimens.

C. A. Hoare.

ABDEL SAYED (Ibrahim). Résumé de sa communication faite le 2 juin 1933 sur l'amibiase.—*C. R. Soc. Méd. et Hyg. Trop. d'Egypte*. Alexandria. 1933–34. 5th Year. Vol. 1. pp. 29–30.

BLANC (F.) & BORDES (L. A.). Considérations pathogéniques et thérapeutiques sur l'amibiase intestinale.—*Marseille-Méd.* 1935. Feb. 5. Vol. 72. No. 4. pp. 145–155.

CHANG (Hsiao-Ch'ien) & CHOU (Shou-k'ai). Amebic Dysentery and its Signoidoscopic Diagnosis.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 433–439. [11 refs.]

FARMAKIDIS (C.). A propos de l'amibiase.—*C. R. Soc. Méd. et Hyg. Trop. d'Egypte*. Alexandria. 1933–34. 5th Year. Vol. 1. pp. 31–34.

FISCHER (Otto). Chronische Darmstörungen und Amöbeninfektion. (Ein Gutachten für die Kriegsbeschädigtenversorgung).—*Muench. Med. Woch.* 1935. Feb. 28. Vol. 82. No. 9. pp. 336–338.

HARGROVE (M. D.). Review of 112 Cases of Amebiasis.—*New Orleans Med. & Surg. Jl.* 1934. Dec. Vol. 87. No. 6. pp. 359–362.

HEGNER (Robert). Absence of Tissue Invasion in Monkey Carriers of *Endamoeba histolytica*.—*Amer. Jl. Trop. Med.* 1935. Jan. Vol. 15. No. 1. pp. 41–43.

IKEDA (Kano). Roentgenologic Observations of the Colon in Amebic Dysentery with Report of Seven Cases Originating in Chicago.—*Radiology*. 1934. May. Vol. 22. No. 5. pp. 610–621. With 7 figs. [12 refs.]

KITABATAKE (Eitaro). Investigations on Amoebic Dysentery. II. Experimental Studies on Amoebic Dysentery in Rats. Part I. Amoebic Dysentery of Rats in the Acute Stadium. *Jl. Oriental Med.* 1934. Oct. Vol. 21. No. 4. [In Japanese pp. 623–652. With 1 chart & 6 figs. on 3 plates. English summary pp. 57–58.]

KITABATAKE (Eitaro). Investigations in Amoebic Dysentery. II. Experimental Studies on Amoebic Dysentery in Rats. Part II. On Amoebic Dysentery in Rats in Chronic Stadium as well as on the Significance of House Rats as Vectors of the Transmission of Amoebic Dysentery.—*Jl. Oriental Med.* 1934. Nov. Vol. 21. No. 5. [In Japanese pp. 827–842. With 7 figs. on 3 plates. [31 refs.] English summary pp. 90–91.]

- KUBO (Michio). Investigations of Amoebic Dysentery. IV. Experimental Studies on Amoebic Dysentery in Dogs. First Report. Amoebic Dysentery of Dogs in Acute Stadium.—*Jl. Oriental Med.* 1934. Dec. Vol. 21. No. 6. [In Japanese pp. 987-999. With 9 figs. on 3 plates. [15 refs.] English summary pp. 113-114.]
- MATHIS (C.). Morphologie et cycle évolutif de l'amibe dysentérique.—Reprinted from *Algérie Méd.* 1931. May. 16 pp.
- MÜHLENS (P.). Folgezustände und Fehldiagnosen nach Amoeben-Dysenterie und ihre Behandlung.—Reprinted from *Tung-Chi Med. Monatsschr.* 1934. No. 5. 12 pp. [In parallel Chinese.]
- PATIÑO MAYER (C.) & GARCÍA ROBIN (Alfredo). Consideraciones sobre un caso de sigmoiditis amebiana crónica, de forma frustra. Resultado del tratamiento arsenical por vía rectal.—*Semana Méd.* 1935. Mar. 21. Vol. 42. No. 12 (2149). pp. 881-884. With 4 figs.
- SABRI (Ismail A.). The Diagnosis of Chronic Dysentery in Children and the Use of the Sigmoidoscope.—*Jl. Egyptian Med. Assoc.* 1935. Feb. Vol. 18. No. 2. pp. 118-124.
- SHATTUCK (George Cheever). Amebiasis in Boston.—*New England Jl. of Med.* 1934. Dec. 6. Vol. 211. No. 23. p. 1044.
- SIMON (Sidney K.). The Clinical Aspects of Amebiasis.—*New Orleans Med. & Surg. Jl.* 1934. Dec. Vol. 87. No. 6. pp. 355-359.
- TANGREDI (Gerardo). Anemia ipocromica grave da amebiasi intestinale.—*Políclinico. Sez. Prat.* 1935. July 1. Vol. 42. No. 26. pp. 1290, 1293-1294. [10 refs.]
- TSUGE (Yukio). Recherches sur la pyogramme entre la dysenterie amibienne et bacillaire.—*Jl. Oriental Med.* 1934. Dec. Vol. 21. No. 6. pp. 95-98. With 12 figs.
- VASILESCU (C.) & PAPAZIAN (R.). Kystes hydatiques suppurés du foie, compliqués d'abcès multiples au foie et péricardite purulente.—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1935. Mar. Vol. 17. No. 3. pp. 40-48.
- YAMAMOTO (Yoshio). Investigations in Amoebic Dysentery. V. On the Cultivation of *Entamoeba histolytica*.—*Jl. Oriental Med.* 1934. Nov. Vol. 21. No. 5. [In Japanese pp. 811-825. With 1 chart. [33 refs.] English summary p. 89.]
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MALARIA.

BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1935. May. Vol. 27. No. 5. pp. 903-929.—Enquête sur les règlements ou prescriptions officielles pour préserver du paludisme les personnes qui se rendent dans des régions malariques: Grande-Bretagne (Colonies Britanniques), Allemagne, Etats-Unis, France (Colonies Françaises et Territoires sous mandat français), Congo Belge, Pays-Bas, Indes Néerlandaises, Italie, Turquie. [**An Enquiry into the Official Regulations and Instructions for protecting from Malaria Persons proceeding to Malarious Countries.**]

The inquiry showed that the counsel generally given to Europeans in different malarious countries was that they should take quinine as a preventive, and should protect themselves against mosquitoes by nets and by proofing their houses. The method of quinine prophylaxis most commonly recommended was a daily dose of 25 centigrams (4 grains), or more rarely 40 to 60 centigrams (6 to 9 grains). In Egypt, Italy and Turkey, the preventive dose of quinine is given on only two days—consecutive or not—in the week. According to the Malaria Commission of the League of Nations, this method is not so efficacious as a small daily dose. The period over which the governments of different countries recommend their subjects to continue taking prophylactic quinine differs in different parts of the world. Europeans in British West Africa are recommended to take quinine daily during the whole of the time they are in Africa, and to continue it for 6 months after their return to England. In French Africa, prophylactic quinine is taken between May and September only. In the Dutch East Indies, quinine is continued for only 2 to 4 weeks after returning to Europe. On German ships, quinoplasmine is used as a prophylactic in preference to quinine. As recent work in England has shown that atebirin is a more potent and less risky prophylactic than plasmoquine, atebirin is to be tested on persons proceeding to West Africa in British ships.

W. Fletcher.

VAN CAMPENHOUT (Em.). La prophylaxie individuelle du paludisme au Congo Belge. [**Personal Prophylaxis in Belgian Congo.**]¹—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 307-309.

Numerous laws are in force with reference to the prevention of malaria which deal with such matters as the provision of mosquito-proofing of houses, collections of stagnant water, accumulations of rubbish, the breeding places of mosquitoes and the like. Government officers are not compelled to take prophylactic quinine but, with rare exceptions, they do so. Medical history records of each officer are kept, and on these a note is made as to the regularity with which they have taken quinine. These records are considered in connexion with leave and pension. All officers on first appointment must attend 17 lectures on tropical hygiene and, during their service, pamphlets on the same subject are issued to them from time to time. Courses of instruction are also available for non-officials. All natives are treated without charge by the Government, and in certain native schools prophylactic quinine is administered regularly.

W. F.

KOMP (W. H. W.) & CLARK (H. C.). **A Fourth Year's Observations on Malaria in Panama, with Reference to Control with Atabrine and Plasmochin.**—*Amer. Jl. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 131-154. [10 refs.]

This is an example of the comparative futility of voluntary drug control, among a native population living in an endemic area.

"During the past 5 years, 1930 to 1934, an area lying in the mid-basin of the Chagres River in Panama has been observed and studied with regard to malaria, and various sorts of treatment have been given the inhabitants in an effort to control the disease. . . . Malaria. . . . cannot be entirely eliminated, but by various means it can be reduced to negligible proportions, as is witnessed by conditions in the Panama Canal Zone, which lies within 7 miles of our towns. The costly measures of control used there are not economically feasible in our area, so our efforts have been directed toward a reduction of malaria, either by direct attack on the parasite by drugs, or by breaking the chain of infection in the mosquito by antigametocyte treatment. Our efforts have been concentrated on . . . the young children . . . We have used several drugs and combinations of drugs over the four-year treatment period. . . . It should be mentioned that all treatment was voluntary. . . . Various combinations of antimalarial drugs were used including quinine sulphate alone or with plasmochin, and atabrine alone or with plasmochin. None of the methods used were particularly successful in reducing the malaria rate, except possibly the combination of atabrine and plasmochin. Monthly surveys over four years indicate the presence of cyclical variations in malaria parasite rate extending over several years. If treatment of any sort happens to be given during a down-swing in rate, success is nearly sure to follow; but if it is given on an up-swing, apparently nothing can stop the natural course of the cycle. . . . Although we feel that the recent improvement in malaria parasite rate is not due solely to our efforts, we have no doubt but that the general health of our villagers is much improved over its condition in 1929, before our work started."

During the course of treating 400 persons with atabrine, no toxic symptoms of any kind were noticed. It was far different with plasmoquine and, when combined atabrine-plasmoquine treatment was given, cases of poisoning were sufficiently common to drive the authors to the conclusion that the toxicity of plasmoquine rendered it unsuitable for mass administration without medical supervision. This is seldom available except in experimental enquiries, and not always in these. The authors regret that it was not available. "Economic considerations overruled in the matter, as we could not afford the expense of maintaining the required supervision." W. F.

DE MELLO (Froilano). Une vue d'ensemble sur la chimioprophylaxie en masse des localités malariennes et ses résultats pratiques. [**Mass Drug Prophylaxis.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 87-92.

The results of mass drug prophylaxis are fairly good if the treatment is continued.

The author first tried the new synthetic drugs in hospital. The results were excellent and the relapses were few, but atabrine proved too expensive for field use. The next step was to try the effect of plasmoquine and quinine in a village. An isolated village was chosen, Paris green was used, adult mosquitoes were killed, the people were kept

under strict control, the drugs were given regularly, and everyone was thoroughly treated. The results were most striking. The spleen rate, in the next epidemic season, was reduced from 82 to 27, and, instead of half the population being incapacitated with malaria, there were only two cases. It would be impossible to impose such rigid discipline upon the general population and the next test was made upon a number of villages where no compulsion was used. Villages with a splenic index above 50 per cent. were given a primary 8-day treatment with plasmoquine and quinine, followed by a secondary treatment consisting of a daily dose and lasting for 12 weeks. Villages with a splenic index between 30 and 50 were given only the primary course. Many people failed to take the treatment, and the results showed that the primary treatment alone was useless. If effort, time and drugs are not to be wasted, it is not only necessary for the primary course to be followed by a secondary course, but the latter must be followed by fortnightly visits to the villages and the treatment of all relapses. W. F.

ISMAİL (Assim). Mesures préventives contre le paludisme dans les régions palustres en Turquie. [**Preventive Measures against Malaria in Turkey.**].—*Bull. Office Internat. d'Hyg. Publique*. 1935. Feb. Vol. 27. No. 2. pp. 304–306.

Quinine prophylaxis is the method adopted for dealing with malaria, and when an area has been declared malarious by the Ministry of Health, certain regulations come into force under a law passed in 1926. The government supplies quinine for labourers on small holdings but, on farms where more than 15 persons are employed, the proprietor must supply 2 grams of quinine per week for each person. If he fails in this, the Health Department steps in and, if he does not pay the bill, he is liable to a fine and imprisonment. W. F.

DUKE (H. Lyndhurst). **Quinine as a Prophylactic in Malaria.** [Correspondence.].—*Lancet*. 1935. Mar. 9. pp. 572–573.

The author complains that in consequence of experiments made in Europe quinine has become discredited as a prophylactic against malaria in tropical countries. "The impression remains," he writes, "that without prophylactic quinine men go down with malaria more often than they used to do under the old rite of 5 grains a day." He does not consider that the results of experiments carried out with European strains of parasites, and with syphilitic patients who have never before suffered from malaria, should be applied to the treatment of patients in the tropics without further inquiry. He suggests that an investigation should be made in Uganda with European and native volunteers. W. F.

DECOURT (P.). Etudes sur la prophylaxie collective du paludisme. [**Mass Prophylaxis.**].—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 176–183.

The author has employed two schizonticidal drugs, quinine and atebirin (or quinacrine), and two gametocidal drugs, plasmoquine (or praequine) and rhodoquine. The objection to quinine was that it had to be given daily. The following doses of the other drugs were given:—Quinacrine 0.4 grams once a week. Praequine 0.03 grams once a week, or Rhodoquine 0.03 grams once a week. Smaller doses were given to children. The results were encouraging. W. F.

DECOURT (P.). Méthode mixte dans la prophylaxie medicamenteuse collective du paludisme. [**Mixed Drug Prophylaxis in Malaria.**]—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 255-261.

A prophylactic mass-treatment with quinacrine and praequine-rhodoquine, given once a week, is recommended. The prophylactic treatment should be begun as soon as the anopheles begin to breed at the commencement of the malaria season. If it is not begun then, and the population is already suffering from malaria, it is necessary to give a preliminary 5-day therapeutic treatment with quinacrine, combined on the first and on the last day with a gametocidal drug. A week later, the prophylactic treatment is begun. This consists of 0.3 grams of quinacrine and 0.02 to 0.03 grams of a gametocidal drug which may be praequine or rhodoquine or a mixture of the two. This treatment is given once a week, during or after food. The doses recommended for children and infants are shown in a table. The method was used with success in a district in the north of Tunis, not far from the Algerian frontier.

W. F.

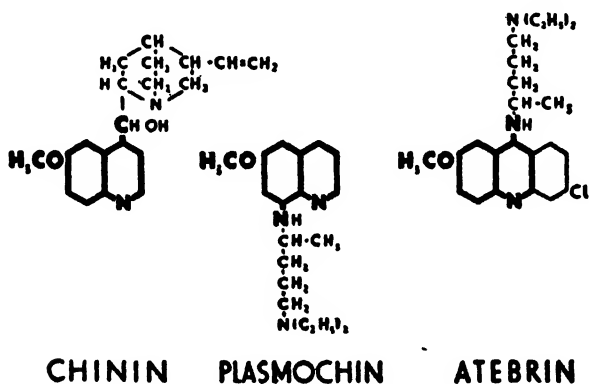
FARINAUD (M. E.). Les possibilités de l'atébriane en prophylaxie collective. [**Atebrin in Group Prophylaxis.**]—*Ann. de Méd. et de Pharm. Colon.* 1934. Oct.-Nov.-Dec. Vol. 32. No. 4. pp. 552-559.

This is a review of observations which have been made—particularly in Malaya by GREEN, WALLACE and KINGSBURY—on the use of atebrin as a prophylactic. In an editorial footnote it is stated that the names "atebrine" and "quinacrine" denote the same drug. The author concludes that on account of the danger of cumulative toxic effects, atebrin should not be placed at the disposal of an ignorant public, but should be given only under medical supervision. He suggests that Europeans are more sensitive to some synthetic drugs than members of coloured races.

W. F.

SCHULEMANN (W.). **The New Synthetic Drugs.**—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 83-88. With 2 charts. [73 refs.]

This lecture was delivered by the author in the Istituto di Malarialogia in Rome. The following diagram of the structure of the three drugs was shown and the lecturer said, "A glance at Chart I will show



you that atebryn, plasmochin and quinine are all derived from 6-methoxy-quinoline which in atebryn is changed to acridin by combining it with a benzol nucleus. The side chains in atebryn and plasmochin are identical, alike in structure and in the nature of the linking member. The positions of the side chains on the ring system differ in plasmochin and quinine, but are analogous in quinine and atebryn." [See HENRY and GRAY, p. 385.]

The author does not consider that final conclusions should be drawn from the results of the treatment of artificially infected syphilitics. These patients are usually infected by the bites of a large number of heavily infected mosquitoes—doses of parasites far greater than they would receive in nature. It might be inferred from the work of CIUCA on general paralytics, and from that of SWELLENGREBEL on very heavily artificially infected volunteers, that the combination of plasmoquine with quinine did not affect the relapse rate; but it has been found at the malaria treatment centre at Kasauli in India, that the relapse rate, which was 70 per cent. with quinine treatment, was reduced to 8.5 with plasmoquine and quinine; eventually the treatment centre was closed for lack of patients. Atebrin does not reduce the relapse rate to quite the same extent as quino-plasmoquine, it is therefore necessary to combine atebryn with plasmoquine, or to give a short course of plasmoquine after the atebryn; in view of the abdominal pains which often occur when the two drugs are given together, the latter course is to be preferred. The author recommends the following treatment for the acute attack (first infection and relapse).

5 to 7 days—0.3 gm. ($4\frac{1}{2}$ grains) atebryn daily.

3 to 4 days—interval.

3 to 5 days—0.03 gm. ($\frac{1}{2}$ grain) plasmoquine daily.

For prevention (general prophylaxis) he recommends 0.02 gm. ($\frac{1}{2}$ grain) plasmoquine on two days in every week throughout the malaria season. Plasmoquine should not be taken on an empty stomach. The rare cases of fatal poisoning have not been due to variations in the toxicity of different samples. AMY has shown that fluctuations in the toxicity of plasmoquine do not occur. "Atebrin does not affect the liver in any way and does not give rise to jaundice." [See DE LANGEN and STORM, *ante*, pp. 726-8.] W. F.

CHOPRA (R. N.), GANGULI (S. K.) & ROY (A. C.). **On the Relationship between the Quinine Concentration in the Circulating Blood and Parasite Count in Monkey Malaria.**—*Indian Med. Gaz.* 1935. Feb. Vol. 70. No. 2. pp. 62-65.

There is no direct relationship between the concentration of quinine in the blood and the number of parasites.

These experiments were carried out on *Silenus rhesus* monkeys infected with *Plasmodium knowlesi*. Quinine was given both intravenously and intramuscularly. The maximum concentration was reached in about 20 minutes and remained fairly constant for about $1\frac{1}{2}$ hours. It was noted that though in some monkeys the maximum concentration was reached in half an hour and was maintained for some time, in others an equally high concentration never developed. The quinine had no visible effect upon the parasites in the blood, no matter how great its concentration. "The infection, as a rule,

was not controlled until 2 or even 3 injections were given at daily intervals, no matter what was the concentration of quinine in the blood. If any change in the parasites was observed, it was an increase in their number immediately after the injection, but never a marked decrease." When once the number of parasites approximated to one million per cmm. no amount of quinine, however administered, was of any avail in saving the monkey. W. F.

CHOPRA (R. N.) & GANGULI (S. K.). **Chemotherapeutic Studies on Plasmodium Infection in Monkeys. No. V. Action of Tebetren.**—*Indian Med. Gaz.* 1935. June. Vol. 70. No. 6. pp. 313-320.

"The drug, it seems, combines the virtues of atebtrin and quinine." But the authors have omitted all reference to trials made elsewhere.

The authors treated with tebetren a number of *Silenus rhesus* which had been infected with *Plasmodium knowlesi*. They conclude that "in so far as the decrease in the number of parasites in the peripheral blood is concerned, tebetren appears to be intermediate in action between atebtrin and quinine. . . . By the intravenous route, . . . its action resembles quinine. So far as relapses are concerned, the effects observed resembled more or less those produced in quinine-treated monkeys." W. F.

LANDEIRO (Fausto). Anreicherungs-methode für die Untersuchung der Malariaparasiten im Blute. [**Enrichment Method for the Detection of Malaria Parasites in the Blood.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1934. June. Vol. 38. No. 6. pp. 253-255.

In the course of the author's work on the sedimentation speed in malaria he used the sediment of the special pipette (Leitz) and the Westergren process for making preparations at different levels of the sedimented blood corpuscles. Parasites were counted in the usual thick drop, in the drops obtained by this process, and also in drops obtained from the lower part of the sediment in the mixing tube of citrate and blood. The drops were examined after an hour's sedimentation.

He examined 117 specimens thus, of which 57 were negative and 60 positive. The parasites stained better and were on a brighter and clearer ground than in the usual drops.

The lower part of the pipette sediment gave preparations 8 times as rich in parasites as the thick drop, the middle part 6 times as rich and the upper part 4 times as rich, while the lower part of the mixing tube sediment gave preparations 6 times as rich as the thick drop. A. G. B.

SINTON (J. A.). **A Method for cleaning the Capillary Tubes used for the Enumeration of Malarial Parasites in the Blood.**—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 1-2.

Capillary vaccine tubes are recommended in place of ordinary capillary pipettes for counting parasites by Sinton's method. If the tubes are thrown away after being used once, this is rather expensive. A method of cleaning them with nitric acid, water and alcohol is described. W. F.

KERIM (M. Abdel). **The Thick Drop Method in the Diagnosis of Malaria.**—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 232–237.

The percentage of positives was increased from 67, found by the thin film method, to 95·5 found by the thick film method. The average time taken in finding parasites was 8·47 minutes in thin films, but only 38 seconds in thick films. W. F.

HOFFMANN (W. H.). Nachweis von Malariaparasiten in schlecht gelungenen Blutaussstrichen. [**Demonstration of Malaria Parasites in Badly made Blood Smears.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 216–217.

In the case of bad blood smears, especially those that are too thick, the author advises that only the thinner part be fixed with methyl alcohol and that the whole smear be stained with dilute Giemsa. The unfixed part, thus freed from haemoglobin, becomes so transparent that even scattered parasites show up clearly. A. G. B.

MENON (T. Bhaskara), KRISHNASWAMY (T. K.) & ANNAMALAI (D. R.). **The Reticulocyte Count in Malaria and Kala-Azar and its Significance.**—*Jl. Indian Med. Assoc.* 1935. May. Vol. 4. No. 9. pp. 359–363. With 5 charts. [13 refs.]

Instead of the ordinary method of taking a drop of blood on to a slide smeared with saturated alcoholic cresyl blue, the authors take up in a pipette, one drop of a 1 per cent. watery solution of cresyl blue and one drop of blood, mix the two drops for half a minute, and then prepare films. In 10 cases of acute malaria, the average reticulocyte count was 1·06 per cent.; in 7 cases of chronic malaria, 3·55 per cent. Cases of kala azar gave an average count of 3·62 per cent. When quinine was given to malaria patients, the count began to rise after 2 or 3 days, and continued to rise for another 2 or 3 days. W. F.

CHOPRA (R. N.), MUKHERJEE (S. N.) & SEN (B.). **Studies on the Protein Fractions of Blood Sera. Part III. Malarial Sera during and after the Rigor Stage.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 571–580. [14 refs.]

The authors' summary is as follows :—

" During the rigor state in malaria the physical properties such as the pH and the buffer action change very little, while the relative viscosity and the surface tension are both lowered, the former to a greater extent than the latter.

" The protein fractions all deviate from the normal, albumin diminishes considerably, the euglobulin increases to a certain extent while the pseudoglobulin remains practically normal. The total proteins also diminish to a considerable extent. In those cases where the blood was drawn after the rigor had subsided the changes in the physical properties and also in the proteins are similar to those of the rigor cases but such changes are less marked and more towards normal.

" From these we are led to conclude that the changes in the physical properties as well as in the proteins of blood sera in malarial patients really set in during the rigor and reach a maximum when these changes begin to disappear and finally reach normal values within a short period after the rigor is over." W. F.

HENRY (A. F. X.). Mélanofloculation en dehors du paludisme et instabilité sérique. [**Henry's Reaction, Melanofloculation without Malaria. Serological Instability.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 14. pp. 1443-1446.

The author discusses the occasional non-specific positive reactions occurring in diseases other than malaria.

Positive results have been reported in kala azar. KAROUT reported positive reactions in rabbits inoculated with typhus virus. His technique was not good; he did not employ formalized controls. TZECHNOWITZER and others reported positive reactions in typhus exanthematicus, but the patients came from malarious places and the typhus may have re-activated their serum. The author has had 4 positive results among 34 rabbits and guineapigs infected with typhus virus. The positive serums contained haemoglobin, and the reaction appeared to be associated with blood destruction. The same occurs, though rarely, in animals infected with trypanosomiasis. The reagents used in Henry's reactions possess certain properties of a colloidal nature which occasionally give reactions obscuring or simulating the specific reaction. The occasional reactions occurring in laboratory animals infected with parasites which destroy the blood cells and produce an instability of the serum do not vitiate the specific reaction which occurs in human malaria. W. F.

TRENSZ (F.). Technique de la sérofloculation palustre par la mélanine choroïdienne purifiée, rendue soluble dans l'eau distillée. [**Henry's Reaction with Soluble, Purified, Choroid Melanin.**—*Arch. Inst. Pasteur d'Algérie.* 1935. Mar. Vol. 13. No. 1. pp. 11-38. With 1 chart. [14 refs.]

The melanin from the choroids of ox's eyes is dissolved in a warm alkaline solution. It is precipitated by acid and then redissolved by alkali. The process is repeated several times, until eventually the precipitate becomes soluble in cold water. This product is as active as the ordinary, untreated melanin, and has the great advantage of being stable. It can be kept for a long time and its activity is constant. In place of the distilled water and the 3 per cent. sodium chloride used by HENRY, the author employs 3 per cent. ammonium chloride, and only two tubes are needed for each test. As the reagent is quite clear, the results are easier to read. The soluble melanin is as sensitive as Henry's reagent, and it gives fewer positive reactions in non-malarial cases. W. F.

TRENSZ (F.). Sur les différences qualitatives qui existent entre les euglobulines du sérum de paludéens et les euglobulines du sérum normal, dans leurs rapports avec la sérofloculation palustre de Henry. [**Henry's Reaction. The Qualitative Difference between the Euglobulins of Normal and Malarial Sera.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 11. pp. 1076-1077.

It has been found that the melanoreaction of Henry depends upon an increase in the euglobulins of the blood. In certain diseases other than malaria the euglobulins are increased and the melanoreaction is positive. Sometimes, where the euglobulin is increased in non-malarious subjects, surflocculance occurs without melanofloculation. The

author has separated the euglobulins from malarial and non-malarial sera by precipitation and dialysis. He has then dissolved them both in serum and in distilled water, and subjected them to Henry's test. As a result he concludes that there are qualitative differences between euglobulins. The euglobulin of malaria possesses a specific character which distinguishes it. (See TRENSZ below.) W. F.

- i. TRENSZ (F.). Des relations qui existent entre les euglobulines et la surfloculation du sérum dans l'eau distillée. [**Henry's Reaction. Euglobulins and Surfloculation in Distilled Water.**—*C. R. Soc. Biol.* 1935. Vol. 118. No. 13. pp. 1332-1333.
- ii. BENHAMOU (Ed.) & GILLE (R.). Les modifications sériques au cours de la malarithérapie.—*Ibid.* pp. 1334-1336.
- iii. THIODET & RIBÈRE. Au sujet de la spécificité et du mécanisme de la réaction de Henry.—*Ibid.* pp. 1336-1338.

i. Surfloculance in distilled water is due to an instability of the serum and to this extent it is related to melanofloculation, but the two phenomena are not identical. Melanofloculation is not due simply to an increase of euglobulin, but to the presence of a special euglobulin. The changes caused by malaria are not merely quantitative, they are qualitative. Certain non-malarial sera which were rich in euglobulins gave a precipitate in distilled water, but not with melanin (*i.e.*, they were "negative"). Part of the precipitate was redissolved in salt solution, and part was added to normal serum. Henry's test was carried out, and again surfloculance occurred, while melanofloculation was still negative although the euglobulin was increased. This procedure was repeated with the precipitate produced in a positive serum by distilled water. Here the redissolved euglobulin gave a positive Henry's reaction because it was malaria euglobulin.

ii. These authors contend that Henry's reaction is not due to a qualitative change in the euglobulin, but to its quantitative increase with reference to serum albumen and cholesterin. A negative malaria floculation signifies that the floculable albumen is maintained in colloidal solution by a sufficient quantity of colloid protectors represented by the serum-albumen and cholesterin. When there is a relative deficiency of these substances, floculation occurs.

iii. Thiodet and Ribère consider that Henry's reaction is of questionable value and non-specific, and that it is due to euglobulin α which is increased in response to all kinds of antigens. A number of cases are cited where patients suffering from diseases other than malaria gave a positive Henry's reaction, for example: pernicious anaemia, lipid nephrosis, starvation, duodenal ulcer, and several other diseases, nearly all associated with anaemia. W. F.

CHORINE (V.) & KOEHLIN (D.). Diagnostic du paludisme par mesure de l'instabilité du sérum dans l'eau distillée. [**Henry's Reaction. Diagnosis by Instability of Serum in Distilled Water.**—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 375-379.

The authors recommend that melanin should be abandoned and that the reaction should be carried out with serum and distilled water.

The results are read with a photometer. The reaction in distilled water shows that titres below 10 indicate the absence of malaria ;

between 10 and 20, doubtful; above 20 almost certain malaria. The reaction becomes negative 30 to 50 days after the institution of effective treatment. The reaction in a group of persons who had returned from malarious countries less than 6 months before being tested proved positive in 50 per cent. The number of positives decreased rapidly during sojourn in a non-malarious country, and fell to 5 per cent. in 2 years. The authors obtained like results when employing melanin, and they conclude that the reaction in distilled water is identical with the melanoflocculation reaction discovered by HENRY. (See pp. 130, 131, 420, 422, above.) W. F.

SINELNIKOW (S. I.), MOLDAWSKAJA-KRITSCHESKAJA (W. D.), GORCHOWA (E. L.), ALTHAUSEN (D. S.) & GRITZAY (A. A.). Vergleichende Bewertung der Melanoflokkulationsreaktionen mit nichterwärmten und auf verschiedene Temperaturen erwärmten Seren. [**Comparative Estimations of the Melanoflocculation Reaction with Unheated and Heated Sera.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 213–216.

An attempt to eliminate non-specific reactions in the melanoflocculation test by heating the serum to various temperatures.

The authors conclude that:—The melanoflocculation reaction carried out with, on the one hand unheated sera, and on the other hand, sera heated for 5 minutes to 54°C. gives concordant results in 85.4 per cent. of definitely diagnosed cases of malaria. If the heating is carried on, under otherwise similar conditions, for 20 minutes then the agreement is only 56.6 per cent. Sera heated to 45° or 50°C. for 5 minutes give the same results as unheated sera. In typhus fever cases, when the sera is heated to 54°C. for 5 minutes the reaction, when positive, is the same in heated and unheated sera, indicating a close connexion in the pathogenesis of malaria and typhus. The authors recommend that the method of carrying out Henry's reaction should be modified, and the sera should first be heated to 45°C. for 5 minutes, because in this method the full specificity of the reaction will be retained, but the possibility of a fallacious, non-specific flocculation will be eliminated. E. D. W. Greig.

SILVESTRINI (R.). Metodo facile di preparazione della sospensione di pigmento corioideo per la melanoreazione di Henry nella malaria. [**Easy Method of Preparation of Choroidal Pigment for Henry's Reaction.**]—*Polislinico.* Sez. Prat. 1935. Apr. 1. Vol. 42. No. 13. pp. 614–615. [13 refs.]

After describing in detail Henry's method of preparing the melanin for his reaction, certain modifications of it and the value and significance of the reaction, the author speaks of a method devised by him, which by its ease of preparation renders the test practicable for any medical practitioner. On the analogy of extraction of the pigment from melanotic tumours by trituration with ether, he suspends the choroidal pigment of the ox in, and treats it repeatedly with, ether in a funnel with a few cubic centimeters of physiological saline. The pigment is deposited in a layer between the saline and the ether. By carefully opening the tap of the funnel, the saline and pigment can be collected

and the ether discarded. Further grinding of the pigment in saline results in a finely opalescent suspension which is distributed in clean tubes and ready for adding to the different dilutions of serum for the test.

By its use the author has obtained marked flocculant precipitation with the sera of malaria patients after 2 hours at 37°C. *H. H. S.*

BENHAMOU (Ed.) & GILLE (R.). A propos du rôle de la cholestérine dans la mélanofloculation (réaction de Henry). [**Henry's Reaction. Cholesterin in Melanofloculation.**].—*C. R. Soc. Biol.* 1935. Vol. 118. No. 15. pp. 1573-1575.

Henry's reaction depends upon an increase of euglobulin, and a diminution of the cholesterin and serum albumen of the blood.

CHORINE and GILLE, on the contrary, found that if cholesterin were added to the serum the intensity of Henry's reaction was increased, and that if cholesterin were removed from the serum, by treatment with ether, it was decreased. The authors state that the added cholesterin does not increase the melanofloculation, but it is precipitated by the addition of water to the serum, and so adds to the opacity. As regards the removal of cholesterin by ether, it is not a reduction in the amount of cholesterin which reduces the flocculability of the serum, but the presence of traces of ether, which act by lowering the surface tension. *W. F.*

KRITSCHESKI (I. L.) & RUBINSTEIN (P. L.). Ueber die Antigennatur des Melanins. [**Antigenic Structure of Melanin.**].—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Apr. 29. Vol. 84. No. 5/6. pp. 397-404.

An experimental study of the nature of the phenomenon of melanofloculation (Henry).

In their investigations the authors employed birds infected with *Plasmodium praecox* and *P. cathemerium*. They obtained the melanin from the choroid of the eye of the ox. They consider that melanin is not a complete antigen, but a hapten and requires the addition of another substance (in the investigation the serum of the pig was employed) to convert it into a complete antigen. They consider that it is highly probable that the phenomenon of Henry in malaria is a reaction between the antigen and antibody and the melanin of the eye of the ox is, from the point of view of antigenic structure, identical with the melanin of protozoa (*plasmodium*). [SINTON & GHOSH consider that malaria pigment is a different substance from melanin. (See this *Bulletin*, Vol. 31, p. 706)]. As a result of their investigations the authors conclude that:—Melanin of the choroid is a hapten, which in the presence of an activator (Schlepper), serum of the pig, is converted into a complete antigen. Similarly the melanin produced by *Plasmodium praecox* is a hapten, whose antigenic completion is effected by an activator, the protoplasm of the protozoa. Henry's phenomenon in malaria is a reaction between antigen and antibody. Melanin differs from all other haptens in being insoluble.

E. D. W. Greig.

SAUNDERS (George M.) & TURNER (Thomas B.). **The Wassermann Reaction in Malaria.**—*Southern Med. Jl.* 1935. June. Vol. 28. No. 6. pp. 542-546. With 1 chart. [12 refs.]

The authors have investigated the Wassermann reaction in malaria, as many have done before, and they conclude that malaria does not cause fixation of complement in this reaction, but that it may stimulate a weak reaction and make it stronger. W. F.

ASCIONE (Guglielmo) & MARIOTTI (Ettore). Esperienze di trasmissione della infezione palustre coi filtrati di sangue e di liquido cefalorachidiano di malarici primitivi. [**The Transmission of Malaria by the Inoculation of Filtered Blood and Cerebrospinal Fluid.**]—*Riv. di Malarologia.* Sez. I. 1935. Vol. 14. No. 1. pp. 1-18. With 7 charts on 4 plates. [14 refs.] English summary.

Particulars are given of 9 experiments in which filtered blood or cerebrospinal fluid was inoculated into healthy individuals. In 5 cases out of 10, this was followed, after 10 to 15 days, by mild accesses of fever. Malaria parasites were not found, but quinine caused the malaria-like syndrome to disappear. [See this *Bulletin*, Vol. 30, p. 487.] W. F.

KNOWLES (R.) & BASU (B. C.). **Nuclear Division in Malarial Sporozoites.**—*Indian Jl. Med. Res.* 1935. Jan. Vol. 22. No. 3. pp. 443-447. With 1 fig. & 1 plate.

Examining sporozoites from the salivary glands of *Anopheles stephensi* infected with *Plasmodium vivax* and *P. falciparum* the author found that the chromatin as seen in dried films stained by Giemsa stain may be present as a single mass or as two or three masses which appear to arise by division from the single one. The appearance is interpreted as indicating nuclear multiplication in the sporozoite.

C. M. Wenyon.

MISSIROLI (A.) & MOSNA (E.). La reazione nucleare nei vari stadi di sviluppo dei parassiti malarici. [**Nuclear Reaction in Various Stages of Development of Malarial Parasites.**]—*Riv. di Malarologia.* Sez. I. 1934. Vol. 13. No. 5. pp. 553-558. English summary (5 lines).

Applying the Feulgen method of staining to human and avian malarial parasites the authors find that a positive result is obtained only with merozoites in the rosette stage and with the oöcysts and sporozoites in the mosquito. In all other stages there was a negative reaction. C. M. W.

IVANIĆ (Momčilo). Ueber die zwei allerfrühesten Kernteilungsstadien des Tertianaparasiten (*Plasmodium vivax* Grassi et Feletti) und deren Bedeutung. [**The First Two Stages of Nuclear Division of *P. vivax*.**]—*Zent. f. Bakt.* I. Abt. Orig. 1935. Feb. 18. Vol. 133. No. 5/6. pp. 274-282. With 11 figs. [13 refs.]

The author has studied the nuclear division in the schizonts of *Plasmodium vivax* fixed both by the dry and the wet methods. The

first two nuclear divisions are at first promitotic, it being possible to distinguish the linin spindle with chromatin granules arranged as an equatorial plate and polar bodies of a plastin nature. As division proceeds the polar bodies are dispersed, the division in its later stages becoming a true mitosis with a granule at each end of the spindle and daughter plates of chromatin substance. C. M. W.

FERREIRA (J. Chaves). Observações sobre os esporozoitos do *Plasmodium praecox* (*relictum*). [Observations on the Sporozoites of *P. praecox*.]—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 5. pp. 559–562. With 35 coloured figs. on 1 plate.

The author has studied the structure of sporozoites of the bird malarial parasite *Plasmodium praecox* in the salivary glands of *Culex pipiens*. It appears that when they first reach the glands each has as a rule a single chromatin mass and a cytoplasm with a neutrophile reaction. During the course of the following 5 or 6 days it appears that the single chromatin mass divides into 8 smaller masses while the cytoplasm at first neutrophile acquires a basophilic and finally an acidophilic reaction. In the last case the sporozoites appear swollen, while the chromatin is disintegrated. C. M. W.

MISSIROLI (A.). Sullo sviluppo dei parassiti malarici. Nota 2a. [Stages in the Life of the Malaria Parasite.].—*Riv. di Malariologia*. Sez. I. 1934. Vol. 13. No. 5. pp. 539–552. With 4 text figs. & 24 figs. on 2 plates (1 coloured). [Refs. in footnotes.] English summary (8 lines).

Professor Missiroli as a result of experiments carried out with *P. praecox* (*relictum*) and canaries finds that sporozoites rapidly disappear from the site of inoculation, in 5–10 minutes in fact. Within the first 5 minutes some at least of the sporozoites will show a swollen nucleus in which are seen 4 or 5 chromatin granules distinct and separate one from another. If later examination, 3 hours or so after, reveals any of them they are only the degenerate or immature. The sporozoites break up into small fragments and are carried off by the lymphatics, in other words they may divide before entering the red corpuscles and do not always penetrate the corpuscle entire and then multiply as described in the text-books. H. H. S.

BLANKENBURG (K.). Experimentelle Versuche ueber die Funktion der Blutreservoirre bei Vogel malaria (*Proteosoma praecox*). [The Function of the Blood Reservoirs in Bird Malaria.].—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 116–121.

It is well known that a large part of the blood of the body is retained in the organs (spleen, bone marrow, liver) as a reservoir where it is in intimate association with the reticulo-endothelial system. In cases of malarial infection large numbers of parasites occur in this reservoir and it would seem that, not completely destroyed by any drugs, they are the forms responsible for relapses. It occurred to the author that methods which bring about a reduction of the blood reservoir and an increase in the blood corpuscles in the peripheral blood might produce a corresponding increase in the malarial parasites. One of these is reduced atmospheric pressure and the author has demonstrated

that malaria infected canaries show an increase in the number of parasites in the peripheral blood if they are exposed to this condition for 5 to 10 minutes. C. M. W.

BRUMPT (Emile). Paludisme aviaire : *Plasmodium paddae* n. sp. du calfat (*Padda oryzivora*). Utilisation de ce parasite pour les recherches chimiothérapiques du paludisme. [*P. paddae* of the Java Sparrow : its Value for Chemotherapeutical Researches.]—C. R. Acad. Sci. 1935. Mar. 11. Vol. 200. No. 11. pp. 967–970. With 24 figs.

The Java sparrow which, as is well known, is frequently found infected with a halteridium (*Haemoproteus orizivorae*) is also liable to a less known plasmodium infection. The plasmodium was actually first seen by ANSCHÜTZ in 1909, who, finding its schizonts associated with the halteridium, thought that these represented an instance of the much talked of schizogony of the female gametocyte. This mistake was, in the author's opinion, again made by LEGROUX and LWOFF. The author and LANGERON studied the plasmodium in 1910 and noted its resemblance to *Plasmodium relictum*. It was not, however, inoculable to the canary or common sparrow. In the present paper the author records these original observations, not published before, and some further ones he has made recently. In spite of its resemblance to *P. relictum* he has not been able to inoculate it to any other bird but the Java sparrow. He gives a figure of the various stages of its development and proposes for it the name *Plasmodium paddae*. He thinks the plasmodium may prove to be useful for testing malarial therapeutic drugs as the Java sparrow is a much stronger bird than the usually employed canary. C. M. W.

BRUMPT (Emile). Paludisme aviaire : *Plasmodium gallinaceum* n. sp. de la poule domestique. [*P. gallinaceum*, n. sp., of the Domestic Fowl.]—C. R. Acad. Sci. 1935. Feb. 25. Vol. 200. No. 9. pp. 783–785. With 18 figs.

In 1912 PROWAZEK briefly referred to a malarial parasite of the fowl in Deli (Sumatra) which gave rise on reproduction to over 24 merozoites. No further reference to this parasite has been made unless the parasite noted by CRAWFORD (1933) in a number of imported fowls in Ceylon and identified by him as *Plasmodium relictum* (*praecox*) is the same species. In 1910 Dr. BROUSSAIS discovered a plasmodium in fowls in Indo-China and was able to inoculate it to other fowls. A film of the blood of an infected fowl was given to the author who now describes the parasite for the first time from this film. It is a large form producing distortion of the cell and displacement of the nucleus. The schizonts produce a variable number of merozoites (7–32), while the gametocytes are relatively large rounded bodies. This parasite, if it were rediscovered, would prove useful for therapeutic experiments. C. M. W.

MANWELL (Reginald D.). Immunity to Cross-Infection in Avian Malaria due to *Plasmodium vaughani*.—Proc. Soc. Experim. Biol. & Med. 1934. Nov. Vol. 32. No. 2. pp. 391–392.

In 1904 NOVY and MACNEAL described as *Plasmodium vaughani* a malarial parasite of the common robin. The author has isolated it in

canaries from a catbird in Syracuse, U.S.A., and has tested its immunity reactions towards other bird parasites. There does not appear to be any cross-immunity between it and other species, not even *P. rouxi* which it resembles morphologically, except that a pre-existing *P. praecox* infection may give a partial immunity to it. On two occasions infected birds seem to have rid themselves entirely of a *P. vaughani* infection, as evidenced by failure of massive doses of the blood to infect clean birds. This is a very rare occurrence in bird malaria.

C. M. W.

MALAMOS (B.) & NAUCK (E. G.). Die Malariaplasmodien der Affen. [**Malarial Plasmodia of Monkeys.**]*—Zent. f. Bakt. I. Abt. Referate.* 1935. Apr. 18 & 25. Vol. 117. Nos. 9/10 & 11/12. pp. 193–218; 241–261. [2 pages of refs.]

In this article the authors give an exhaustive account of the malarial parasites of monkeys based on a detailed analysis of the literature, complete references to which are given. Not only are the parasites of the Old World monkeys dealt with, as in the recent publications of SINTON and MULLIGAN which are repeatedly referred to, but those of the New World are also considered, while the parasites of the higher apes are fully described. The article cannot fail to be of the greatest assistance to all who wish to study malaria as it occurs in monkeys.

C. M. W.

MULLIGAN (H. W.). **Descriptions of Two Species of Monkey Plasmodium isolated from *Silenus irus*.***—Arch. f. Protistenk.* 1935. Vol. 84. No. 2. pp. 285–314. With 2 charts & 2 coloured plates. [26 refs.]

Much of the information contained in this paper has already been published by the author in collaboration with SINTON. It gives, however, a descriptive account of *Plasmodium knowlesi* and *P. cynomolgi*, both of which together with *P. inui* (described by SINTON, see below) occur as natural infections in the monkey *Silenus irus* (*Macacus cynomolgus*). The paper is illustrated by two excellent coloured plates showing the characters of the two parasites. Some reference is also made to *P. inui*, and its cycle of development is given as 48 hours while in the later paper by SINTON, based probably on more extended observations, the figure is 72.

C. M. W.

SINTON (J. A.). **A Quartan Malaria Parasite of the Lower Oriental Monkey, *Silenus irus* (*Macacus cynomolgus*).***—Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 379–410. With 79 coloured figs. on 2 plates & 1 chart. [31 refs.]

The author describes the isolation in pure culture of a third malarial parasite from the monkey *Silenus irus*. Hitherto two species have been isolated, *Plasmodium knowlesi*, Sinton & Mulligan, 1932, with a 24-hour periodicity, and *P. cynomolgi*, Mayer, 1907, with a 48-hour cycle. The former produces a maximum of 11 merozoites, does not enlarge the red cell and produces a stippling demonstrable only by special staining, while the latter produces up to 16 merozoites, enlarges

the red cell and gives rise to conspicuous stippling. The new parasite, which has been identified with *P. inui*, Halberstadter & Prowazek, 1907, has a cycle of 72 hours, enlarges the red cell slightly, produces stippling which is less conspicuous than that caused by *P. cynomolgi* and produces up to 16 merozoites. These 3 malarial parasites occur naturally in *Silenus irus* very commonly in mixed infections. They do not produce any serious symptoms in the natural host nor do *P. inui* and *P. cynomolgi* in other species of *Silenus* to which they are inoculable. On the other hand *P. knowlesi* is highly pathogenic for *S. rhesus*, in which it gives rise to a severe disease often associated with haemoglobinuria. The *Silenus irus* in which the 3 parasites were found had come to India from Malaya. It appears that *P. inui* is identical with the parasite described by HALBERSTADTER & PROWAZEK (1907) from *S. irus* from Java and *S. nemestrinus* from Sumatra and Borneo and with the form seen by MATHIS & LEGER (1911) in *S. rhesus* and *S. lasiotis tcheliensis* from Tonking. Thus *P. inui* has a wider distribution than the other 2 species which at present are known only from Malaya.

The following table taken from the paper gives the differential characters of the 3 parasites.

	<i>Pl. inui</i>	<i>Pl. cynomolgi</i>	<i>Pl. knowlesi</i>
Natural hosts ...	<i>Silenus irus</i> <i>S. nemestrinus</i> <i>S. rhesus</i> <i>S. lasiotis tcheliensis</i>	<i>S. irus</i>	<i>S. irus</i>
Regions from which recorded	Borneo, Java, Sumatra, Tonking, Malaya	Malaya	Malaya
Duration of schizogony cycle	72 hours	48 hours	24 hours
Chromatin in young ring forms	Frequently double and of very unequal size	'Accessory dot' present	'Accessory dot' present
Trophozoites ...	Amoeboidicity of lobose nature; vacuolation marked up to early segmentation	Amoeboidicity marked, of 'vivax' character; vacuole at first well developed but not marked in old forms	Amoeboidicity slight or absent; vacuole small in older forms
Pigment in trophozoites	Yellow to brown, becoming darker with age; appears early; fine and abundant with peripheral distribution	Golden-brown; appears later and is coarser and scantier than in <i>Pl. inui</i> ; distribution less markedly peripheral	Golden-brown to almost black; appears early; abundant
Mature schizonts...	Maximum 16 merozoites. Often rosette	Maximum 16 merozoites. More irregular	Maximum 11 merozoites. Grape-like cluster

	<i>Pl. inui</i>	<i>Pl. cynomolgi</i>	<i>Pl. knowlesi</i>
Gametocytes ...	About size of normal red cell; pigment scattered, yellowish brown to brown and abundant	Distinctly larger than red cell; pigment not very abundant; darker than in <i>Pl. inui</i>	About size normal red cell; pigment relatively coarse, brown to black, and abundant
Infested red cells ...	Slightly enlarged with older forms. Stippling less conspicuous, scantier than with <i>Pl. cynomolgi</i>	Much enlarged with old forms. Stippling very conspicuous and dots very numerous	Not enlarged; showing characteristic distortion. Stippling only shown by special stains
Pathogenicity ...	Few or no symptoms. Easily inoculable to other species of <i>Silenus</i> . Not inoculable into higher monkeys	Usually no severe symptoms. Easily inoculable to other specimens of <i>Silenus</i>	Mild in <i>S. irus</i> , but causing very severe symptoms, often haemoglobinuria, when inoculated into <i>S. rhesus</i> . Has been transmitted to man and the gibbon

C. M. W.

KNOWLES (R.) & GUPTA (B. M. Das). **Latent Malaria Infection in Monkeys.**—*Indian Med. Gaz.* 1934. Oct. Vol. 69. No. 10. pp. 541-545. With 3 figs.

A specimen of *Silenus irus* on which splenectomy had been performed followed by inoculation with a pure strain of *Plasmodium knowlesi*, developed an intensive malarial infection in which not only the inoculated parasite but also *P. inui* var. *cynomolgi* was present. The operation of splenectomy appeared to have re-awakened a latent infection. To test the matter further a series of 5 young *Silenus irus* were subjected to careful examination. Thick and thin films were examined daily for 10 days. The result was the discovery of parasites in two. An attempt to arouse infection in the others by injection of 2 cc. of horse serum failed. Then 2 cc. of blood from each of the negative monkeys was inoculated into susceptible *S. rhesus*, with the result that one became infected, showing that one of the 3 negative *S. irus* had a very slight infection. The 3 monkeys were then subjected to splenectomy, with the result that malarial parasites appeared in the blood of all. It appears, therefore, that the most certain method of detecting a latent malarial infection is by splenectomy.

C. M. W.

NAUCK (E. G.) & MALAMOS (B.). Ueber Immunität bei Affenmalaria. [**Immunity in Monkey Malaria.**—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1935. Mar. 4. Vol. 84. No. 4. pp. 337-358. With 6 figs.

In the investigations described in this paper the author has followed the development of immunity in monkeys inoculated with *Plasmodium knowlesi*. Three different monkeys were used (*Silenus rhesus*, *S. irus* and *Cercopithecus mona*) and it was found that they differed from one another as regards reaction to the infection and the rate of development of immunity, which was of two types. That to develop first was a toxin immunity or an immunity which enabled the animal to tolerate the parasites present in the blood. Later there developed in addition to this a parasite immunity which enabled the animal to suppress the parasites by getting rid of them entirely or by keeping them in abeyance. Though from the point of view of the development of immunity the spleen is very important it is not absolutely necessary, for immunity will develop in splenectomized animals though more slowly than when this organ is present. The removal of the spleen in an already immune animal lowers the immunity to some extent. The existence of acquired immunity is not entirely dependent on the presence of a latent infection (premunity) since it may exist when, as tested by every available means, the monkey appears free from parasites. C. M. W.

CHAND (Khazan) & HARBHAGWAN. Some Unsuccessful Attempts to transmit Monkey Malarial Parasites to Common Laboratory Animals.—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 373-378.

An attempt to infect the rabbit, guineapig, rat, mouse, squirrel and dog with one or other of the three malarial parasites (*Plasmodium knowlesi*, *P. inui*, *P. cynomolgi*) of the monkey *Silenus irus* (*Macacus cynomolgus*) has completely failed. C. M. W.

PITTI-FERRANDI (François) & SAUTET (Jacques). Anophélisme sans paludisme dans un village corse de montagne. [**Anophellism without Malaria in a Corsican Mountain Village.**—*Rev. Méd. et Hyg. Trop.* 1934. Nov.-Dec. Vol. 26. No. 6. pp. 262-267.

The village of Pietra-di-Verde with some 700 inhabitants is situated about 15 kilometres from the east coast of Corsica, at an altitude of 500 metres. It used to be malarious, but, since 1925, there has not been a single local case in spite of the continual importation of parasites by villagers returning from the plains. This change is not due to the deviation of the anopheles by an increase of domestic animals: there are fewer animals than in the past, and mules—the only ones which were stabled—have been largely replaced by motor transport. The larvae of *A. maculipennis* and *A. bifurcatus* are plentiful, but the adults do not come into the houses to feed, and people sleeping in rooms with open windows, close to the breeding-places, are never bitten. The mosquitoes probably feed on the domestic animals which are turned loose in the woods, for they are not plentiful in the stables. The local *A. maculipennis* appears to be a small, paucidentate race. One of the authors has carried out a vigorous quinine treatment of all cases of malaria for a number of years, and there have been fewer imported

cases, but these factors are not sufficient to account for the disappearance of the disease, because in neighbouring villages in the plains, where the same has been done, malaria has not disappeared. W. F.

- i. TREILLARD (M.). Gîtes, sites ou régions, dans la localisation des espèces anophéliennes de l'Indochine méridionale. [**Breeding-places, Sites or Regions in the Localization of the Anophelines of Southern Indo-China.**]—*Bull. Soc. Path. Exot.* 1935. Jan. 9. Vol. 28. No. 1. pp. 40–42.
- ii. —. Tableau synoptique pour la détermination rapide des anophèles d'Indochine. 2. Larves. [**A Synoptic Table for the Rapid Determination of the Anopheles of Indo-China. 2. Larvae.**]—*Ibid.* pp. 42–44. With 1 fig.

i. The species of *Anopheles* having been identified, we need to know as definitely as possible where and when they are to be found. As yet, however, breeding-places cannot be determined precisely, since we are still ignorant of too many of the factors governing their selection by the female mosquitoes, and the subsequent development and fate of the progeny. The real characteristics which make a breeding-place attractive to female *Anopheles* do not necessarily affect its topography, and may be incommunicable by means of description or photographs. On the other hand no appreciable results have been obtained by studying either the microflora, microfauna or physico-chemical qualities of water, although recent investigations by MORIN and BADER (see this *Bulletin*, Vol. 31, p. 718) seem to indicate a suggestive simultaneity between certain percentages of carbonic acid and the presence of larvae of *A. minimus*. To avoid serious errors we must confine ourselves to broad categories (running and stagnant water, spring water and salt, water but slightly or heavily charged with organic matter, etc.), and to the idea of larger or smaller faunal regions, within which every collection of water is more or less suspect. Moreover it must not be forgotten that the biological needs of the adult are just as important as the physiological necessities of the larva.

ii. The table provided is on the lines of that recently given by the author for the adults of the species included (this *Bulletin*, ante, p. 438), but the characters are indicated in a purely schematic and conventional manner by means of blank or shaded spaces. Intended primarily for the use of beginners, this method of determination may have a certain value, but accurate results are unlikely to be obtained without practice, and larvae for examination will be better dead than alive.

In a list of twenty-one species of *Anopheles* met with in Indo-China between January and September, 1932, the following are shown as harbouring malaria parasites in the south :—*A. hyrcanus*, *A. minimus*, *A. aconitus*, *A. jeyporiensis*, *A. ludlowi*, *A. leucosphyrus* and *A. kochi*.

E. E. Austen.

GASCHEN (H.). Sur un nouvel agent transmetteur du paludisme en Indochine septentrionale *Anopheles culicifacies* Giles 1901. [***A. culicifacies* as Malarial Vector in Indo-China.**]—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 111–113. [10 refs.]

The presence of *A. culicifacies* in Indo-China was first notified in 1932 by TOUMANOFF and FARINAUD. The author captured a specimen in

1934 at Lahati (Yunnan) with oöcysts in the gut. It probably acts as a vector in the highlands and is responsible for the generalized malaria of mild type in such areas as the plateaux of Yunnan, where the only other anopheles are *A. sinensis* and *A. vagus*. W. F.

GASCHEN (H.). Recherches entomologiques dans la province du Yunnan. [**Entomological Investigations in the Province of Yunnan.**]—*Bull. Soc. Méd.-Chirurg. Indochine*. 1934. Nov. Vol. 12. No. 9. pp. 873-892. With 1 folding chart. [14 refs.]

——. Faune entomologique des voies d'accès au Yunnan. [**Entomological Fauna of the Approaches to Yunnan.**]—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 194-198.

The province of Yunnan, situate in the extreme south-west of China, is a high plateau, traversed fan-wise by several mountain chains, and by large rivers running from west to east and south. Investigations into its anopheline fauna made by MORIN in January, 1934, were followed by others conducted by the author in the ensuing August and September. Eleven species of *Anopheles* were met with, viz. :—*A. sinensis*, *A. vagus*, *A. culicifacies*, *A. minimus*, *A. jeyporiensis*, *A. lindesayi*, *A. maculatus*, *A. aitkeni*, *A. barbirostris*, *A. gigas* and *A. kochi*—all, with the exception of *A. lindesayi* of which adults alone were found, in both larval and adult stages. *A. culicifacies* and *A. gigas*, until encountered by the author, had not been taken in Yunnan; a specimen of the former, caught at Lahati, contained oöcysts in the stomach-wall. In the vicinity of Yunnanfou *A. sinensis* was found breeding at an altitude of some 2,400 metres (nearly 8,000 feet).

Phlebotomus (*Ph. barraudi*) was captured in the province for the first time. E. E. A.

FENG (Lan-chou). Notes on Some Mosquitoes collected from Shantung Province, North China.—*Chinese Med. J.* 1935. Apr. Vol. 49. No. 4. pp. 359-365.

The author cites three papers about anopheles in Shantung, by CHRISTOPHERS, HINDLE and himself. He himself has made several collections of mosquitoes since 1927; they contain 15 species, 3 of which are anopheles, 4 aëdes and 8 culex. A short description is given of each with notes on their habits. *A. hyrcanus* var. *sinensis* is the most common anopheles both in the plains and hills and has been shown by HINDLE and Feng to be infectible with *P. vivax*. *A. lindesayi* var. *japonicus* is rare, and it is not known whether it bites man. *A. pattoni* is common in the hills and will harbour *P. vivax*. A. G. B.

PETRISHCHEVA (P. A.). Zur Fauna und Biologie der Culicidae des Karakala-Gebietes. [**Contribution to the Fauna and Biology of Culeids of the Karakala Region.**]—*Trud. Karakal. i Kzui-Atreksk. parazit. Eksped. 1931 i Mater. po Faune Turkm.* in *Trud. Sov. Izuch. proizv. Sil*, Ser. turkmensk. Leningrad, Acad. Sci. 1934. Pt. 6. pp. 85-104. With 6 figs. & 1 graph. [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. pp. 73-74.]

"The 15 species of mosquitos found in the Karakala region (south-western Turkmenistan) in 1930 included 6 of the genus *Anopheles*, viz., *A. superpictus*, Grassi, which was the most common, *A. maculipennis*, Mg., *A. claviger*, Mg. (*bifurcatus*, auct.), *A. hyrcanus* var. *pseudopictus*, Grassi, *A. pulcherrimus*, Theo., and *A. plumbeus*, Steph. The last three were

rare. Notes on the breeding-places are summarised in a table. Larvae of *A. superpictus* occurred from May till the end of November in almost all types of water, especially in spring water exposed to the sun, along the pebbly banks of rivers and streams, and in flooded areas with a very slow current and sparse vegetation. They were often found, together with those of *A. claviger*, in wells in which the water was very high, and in one instance larvae, pupae and empty pupal skins occurred in a deep well situated in a gloomy mine gallery. As the walls of the well were of hard rock and there was no vegetation, the author believes that the larvae of *A. superpictus* can develop on the colloid substances dispersed in water if coarser particles in suspension are absent. Larvae of *A. claviger*, which were found throughout the year, occurred in a variety of breeding-places, including water exposed to the direct rays of the sun, streams almost hidden in dense grass, and in one instance water from a sulphur spring devoid of macroscopic organic matter. Larvae of *A. maculipennis* occurred from May till the end of November in large shallow accumulations of water formed by the overflow of irrigation ditches and covered with grasses, and sometimes along pebbly river banks.

"The adults of *A. superpictus* were predominant in dwellings and out-houses, while *A. maculipennis* occurred much less frequently, and *A. claviger* very rare. On the whole, mosquitos were most numerous in gorges, caves and burrows of animals, reeds, etc., at a distance of from 6 to 25 miles from human habitations. *A. superpictus*, which was again predominant, was found at altitudes up to 6,500 ft., *A. claviger* up to 5,000 ft. and *A. maculipennis* up to 2,500 ft., while other Anophelines occurred in valleys up to an altitude of 1,600 ft. The adults of *A. superpictus* and *A. maculipennis* were found throughout the year, the former being most numerous in August and September. *A. claviger* was obtained from April to the end of November, *A. hyrcanus* var. *pseudopictus* from June to the end of August, and *A. pulcherrimus* in July and August only."

RUSSELL (Paul F.) & BAISAS (Francisco E.). **Habitats of Philippine Anopheles Larvae.**—*Philippine Jl. Sci.* 1934. Dec. Vol. 55. No. 4. pp. 297–306. With 5 plates. [15 refs.]

Although the genus *Anopheles* is abundantly represented in the Philippine Is., comparatively little is known of the bionomics of the local species, of which, to the extent indicated in the title, the present paper, "based on collections made by the staff of Malaria Investigations from January, 1930, to September, 1934, in every province in the Philippines under varying conditions as to altitude, type of breeding place, and time of year," provides a useful summary. In addition to original observations, earlier reports by other writers have also been utilized. The breeding-places of no fewer than twenty-seven species or varieties, two of which have not been precisely identified, are noted and in some cases illustrated. Breeding habits in the same species often vary widely, and on the other hand observed preferences are difficult to explain. *A. minimus* var. *flavirostris*, "the chief malaria vector in the Islands, . . . breeds particularly in foothill streams along the shaded edges, especially among bamboo roots." E. E. A.

SEN (Purnendu). **Anopheles Breeding in Relation to Rice Cultivation in Lower Bengal.**—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 97–108. With 8 charts. [12 refs.]

"Every area of cultivation must be judged on its own merits."

Certain municipalities prohibit cultivation within half a mile, or a mile, of their town or village, but this is not always necessary. Three

villages surrounded by rice fields, within 12 miles of Calcutta and typical of lower deltaic Bengal, were chosen for observation. Nearly 50 per cent. of the mosquitoes breeding in the rice fields were *A. hyrcanus* var. *nigerrimus*; *A. culicifacies* was not found. *A. philippinensis* was found in some of the fields, but not in large numbers, and two other carriers, *A. varuna* and *A. annularis*, occasionally. One of the villages was malarious, with a spleen rate of 50 per cent.; one was slightly malarious, with a spleen rate of 10 per cent.; the third was healthy, and its spleen rate was nil. In this last village, the water of the paddy fields had a higher salinity, and *A. philippinensis* did not breed there. The author concludes that "It does not appear that there is any direct correlation between the malariousness of a place and rice cultivation in lower Bengal."

W. F.

MEASHAM (J. E.) & CHOWDHURY (M. U.). **A Note on the Anopheline Mosquitoes of the Anaimallai Hills.**—*Records of the Malaria Survey of India*. 1934. Dec. Vol. 4. No. 4. pp. 363-365.

The Anaimallai Hills are the tea planting district of the western Ghats, 10 degrees north of the Equator. The estates lie at an elevation of 3,000 to 4,000 feet, surrounded by hills 5,000 to 8,000 feet high. *A. fluviatilis* was the only anopheline found to be infected; it breeds in the grassy edges of slow-running streams where shade is not too dense. From June to October, the rivers are in flood and anopheles cannot be found in them. The malaria transmission season lasts from March to June and, during those 3 months, 8.86 per cent. of the *A. fluviatilis* were found to be infected. Counts were made of adults caught in stables and dwellings, which showed the androphilic character and prevalence of *A. fluviatilis*. These are some of the figures:—*A. fluviatilis*, 199 in dwellings, 4 in cattle sheds; *A. maculatus*, 14 in dwellings, 34 in cattle sheds; *A. vagus*, 12 in dwellings, 123 in cattle sheds.

W. F.

i. EVANS (A. M.) & LEESON (H. S.). **The *Funestus* Series of *Anopheles* in Southern Rhodesia, with Description of a New Variety.**—*Ann. Trop. Med. & Parasit.* 1935. Apr. 25. Vol. 29. No. 1. pp. 33-47. With 10 figs. [12 refs.]

ii. LEESON (H. S.). **Another Anopheline of the *Funestus* Series from Southern Rhodesia.**—*Ibid.* pp. 69-71.

i. In Southern Rhodesia, what a few years ago would have been regarded simply as *Anopheles funestus* now proves to consist of:—*A. funestus* (*typicus*), *A. lesoni* (described in 1931 as a subspecies of *A. funestus*, but in this paper raised to specific rank), and a new variety here characterized as *A. funestus* var. *confusus* var. nov. The main distinctive characters of all three of these, in their different stages, are stated in the text, shown in tabular form and displayed in the figures. Notes on distribution in S. Rhodesia, and on bionomics are added. Adults of all three, which breed at the edges of sluggish streams and in swamps, occur in houses. Out of doors their favourite retreats along streams are among grass and weeds, in crevices and cavities in the soil, and beneath stones at "drifts"; they likewise lurk in disused quarries and gravel-pits.

ii. *A. funestus* var. *rivulorum* var. nov., here described, is an addition to the foregoing. The egg has not so far been identified, but

the larvae, which in the shape and size of the main tergal plates resemble those of *A. longipalpis*, occur "in slowly moving streams near banks and among boulders," with those of *A. funestus* var. *confusus*, *A. lesoni*, *A. longipalpis* and *A. pretoriensis*. The adults are found "along streams, in crevices and cavities in the banks."

E. E. Austen.

AMBIALET (R.). Activité anophélienne et conditions climatiques sur le littoral algérien. [**Anopheline Activity and Climate on the Algerian Coast.**]*—Arch. Inst. Pasteur d'Algérie.* 1935. June. Vol. 13. No. 2. pp. 201–204. With 1 map, 1 chart & 4 figs. on 2 plates.

A village near Constantine with much malaria was selected for these trials. Traps of metallic gauze, such as are set in the apertures of doors and windows, baited with rabbits were arranged and were emptied twice a week for a year, while observations were made of maximum and minimum temperature, rainfall, fog, wind, etc. The result is shown graphically. In the traps were collected female *A. maculipennis* (and one male) and female *Culex pipiens*, which seemed to show that the insects entered for blood rather than shelter. The graph shows parallelism between captures of *Anopheles* and *Culex* and the importance of seasonal variations in the activity of mosquitoes. They were active at two periods—from May 26 to July 10 and from September 1 to November 20, *i.e.*, between the minimum and maximum of 10° and 30°. The great heat in summer was as inimical to them as the cold of winter.

A. G. B.

VILLAIN (Georges), DUPOUX (Robert) & MARINI (Charles). Contribution à l'étude de l'anophélisme tunisien et aperçu de la lutte antianophélienne dans la régence. [**Anophellism in Tunis, with Sketch of the Anti-Mosquito Campaign in the Protectorate.**]*—Arch. Inst. Pasteur de Tunis.* 1935. Apr. Vol. 24. No. 2. pp. 309–342. With 12 figs.

The first part of this paper consists of a list, in tabular form and in many cases giving details as to vegetation, etc., of *Anopheles* breeding-places in Tunis, all of which have been inspected and verified by the authors, while the larvae found have been carefully determined. The species met with are:—*A. maculipennis*, which occurs more or less everywhere; *A. hispaniola*; *A. multicolor*; *A. algeriensis*; *A. sergenti* and *A. superpictus*. *A. bifurcatus*, *A. marteri*, *A. broussesi* and *A. elutus*, although occurring in Algeria, have not so far been encountered. The importance of wells as anopheline breeding-places is emphasized; but abandoned wells, or modern ones fitted with wind-pumps, are more dangerous than those of the Arab type, in which the water is frequently and violently disturbed by buckets.

A. maculipennis appears to show a marked preference for human blood, and GALLIARD (see below, p. 813) from an examination of eggs and larvae from various regions in Tunis, considers that all those collected belong to var. *labranchiae*. In winter, at least in certain specified regions, the adult females take refuge in houses and pass into semi-hibernation, *i.e.*, they remain active and ready to feed, but do not go outside in order to oviposit.

Anti-mosquito measures on a large scale, for which the necessary funds and personnel are now available, and of which some details are given, have been in operation in Tunis for scarcely five years. As regards biological control, very satisfactory results have been obtained from stocking with top-minnows (*Gambusia holbrooki*), which are among the most valuable auxiliaries in attacking anopheline larvae. Reliance is also placed on oiling, and Paris green, for the dissemination of which an aeroplane proved to be too costly in material, is employed only for broad, grass-grown expanses. E. E. A.

DUNN (Lawrence H.). **Entomological Investigations in the Chiriqui Region of Panama.**—Reprinted from *Psyche*. 1934. Vol. 41. No. 3. pp. 166–183.

The greater part of this paper is concerned with animal and bird parasites, but there are a few notes on mosquitoes (*Anopheles albi-manus*, *A. punctimacula* and nine culicines), and on species of *Simulium* and Ceratopogonidae (*Culicoides* and *Lasiohelea*) attacking man. The majority of the culicines met with were found breeding, but no anopheline larvae were discovered. Specimens were collected on three different occasions, but the investigations appear to have lasted only a few weeks. E. E. A.

BOYD (Mark F.), CAIN (T. L.), Jr. & MULRENNAN (J. A.). **The Insectary Rearing of *Anopheles quadrimaculatus*.**—*Amer. Jl. Trop. Med.* 1935. May. Vol. 15. No. 3. pp. 385–402. With 7 figs.

This is a detailed description of the type of outdoor insectary used in Florida, and an indoor insectary in New York, for rearing *Anopheles quadrimaculatus* and *A. punctipennis*.

The same methods with very slight modifications serve for the two species; more extensive modifications are probably required for *A. crucians*. Photographs and plans of both insectaries are given. In Florida the natural conditions of temperature and humidity are satisfactory; in New York, by means of a Frigidaire air-conditioning unit, the temperature is kept always at about 72°F. (22°C.) and by introducing water vapour from the hot water supply, a relative humidity of about 70 per cent. is maintained. In the belief that ultra violet rays are essential to proper larval development, these are supplied two hours daily from a lamp. The larvae are reared in enamelled pans 12 inches in diameter and 2½ inches deep, and fed on hay infusion with strips of cork floating on the surface. The adults are fed on man. The many empirical details as regards the preparation of the hay infusion, etc., must be read in the original. Colonies of 3,000–5,000 are maintained. V. B. Wigglesworth.

BARBER (M. A.). **Malaria Studies in Greece. A Method of detecting the Eggs of *Anopheles* in Breeding Places and Some of its Applications.**—*Riv. di Malarologia*. Sez. I. -1935. Vol. 14. No. 2. pp. 146–149. English summary (5 lines).

A thumbless mitten or bag of white muslin is worn on the left hand. The surface of the water is skimmed with a pan and the contents of the

pan are strained through the mitten. The material collected on the mitten is examined with a hand lens. A good combination of lenses for field use is a 7X and a 20X. If it is desired to take eggs to the laboratory, several mittens can be used, or squares of muslin may be employed to place over the glove. The mittens, or the squares, can be put into flat boxes with the eggs on them for transport to the laboratory.

W. F.

RICE (J. B.) & BARBER (M. A.). **Malaria Studies in Greece. A Modification of the Uhlenhuth-Weidanz Precipitin Test for determining the Source of Blood Meals in Mosquitoes and Other Insects.**—*Jl. Lab. & Clin. Med.* 1935. May. Vol. 20. No. 8. pp. 876-883. With 6 figs.

This is a detailed account of the test illustrated with photographs and diagrams. It should be read by those who wish to carry out precipitin tests on mosquitoes.

The authors obtained precipitating sera for man, sheep, horse, pig and cow in ampoules from the Istituto Sieroterapico of Milan, Italy. These were diluted with seven parts of the following diluent :—

Sodium chloride	4.25 gram
Glycerine	166.00 c.c.
Phenol	2.50 "
Distilled water	330.00 "

The diluted sera will keep 10 months, overlaid with paraffin in the ice-box. One cubic centimetre of undiluted serum is sufficient for the testing of 700 mosquitoes. The fresher the blood to be tested the better. The blood inside a mosquito often becomes black and unfit for the test in 24 hours if the weather is hot. The authors put their collections of mosquitoes in corked, labelled test-tubes; the tubes are placed in a large thermos jug with abundance of ice for transport to the laboratory. It is best to remove blood from the mosquito to filter-paper on the same day, but, with a well-iced thermos jug, this may be postponed for 24 hours. Round, hard, filter-paper, 9 cm. in diameter (Whatman No. 5) is used. The mosquitoes are lightly chloroformed, and the blood from each stomach is expressed on to the margin of the filter-paper; labels are written in the middle. Dried blood specimens can be kept for months in a cool, dry place. Each blood spot is cut out for testing, and dissolved in 3 cc. of salt solution. The blood spots are allowed to soak in the salt solution for an hour at room temperature in order to extract the serum. The actual tests are made in capillary tubes, 6.5 cm. long with an internal diameter of 2 mm. A description is given of the manipulation of these tubes and of the method by which they are cleaned.

W. F.

MISSIROLI (A.). Osservazioni sulla biologia dell'*Anopheles plumbeus*. I Nota. [On the Biology of *Anopheles plumbeus*. Preliminary Note.]—*Riv. di Malariologia*. Sez. I. 1935. Vol. 14. No. 2. pp. 150-154. With 2 figs. English summary.

The author states that the "negative phototropism" of larvae of *A. plumbeus* is known and that the same avoidance of light guides the

adult in selecting the site for depositing her eggs. He found numerous larvae in shaded cavities in rocks where clean rainwater was collected, but from other collections fed by springs and exposed to light they were absent. He agrees with ROUBAUD that the larvae of winter generations possess a remarkable reserve of fat and develop slowly regardless of the environmental conditions. *H. H. S.*

- PUNTONI (V.). Sur le développement des larves d'anophèles dans les eaux d'égout. [**The Development of Anopheline Larvae in Sewage.**—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia.* Milan. 1934. May. Vol. 6. No. 5. pp. 161-164.
- . Azione delle acque di fogna sullo sviluppo delle larve anofeline. —*Riv. di Malarologia.* Sez. I. 1934. Vol. 13. No. 6. pp. 721-733. French summary.

In view of the general belief that anophelines, as opposed to culicines, need clean water for their development, the author set himself to determine whether irrigation with sewage would be likely to prove a useful method in a campaign against the former. Unfortunately the outcome of his experiments, in which he used larvae of *Anopheles maculipennis*, vars. *labranchiae* and *messeae*, and various dilutions of sewage as media, appears to show, not only that there is no foundation for the popular idea in question, but also that the employment of sewage as a fertilizer would actually accelerate *Anopheles*-breeding, and would increase the proportion of larvae which arrive at maturity. *E. E. Austen.*

- MEHTA (Dev Raj). Effect of "Saline and Free" Ammonia on the Oviposition of *Anopheles culicifacies* and *Anopheles subpictus* (Rossi).—*Records of the Malaria Survey of India.* 1934. Dec. Vol. 4. No. 4. pp. 411-420. With 1 chart. [20 refs.]

The author wishes to define the concentrations of ammoniacal materials which prevent the oviposition of two common Indian Anophelines.

The greater part of the work was done in cages containing vessels holding natural waters of different ammonia concentration, or else solutions of ammonia salts prepared in the laboratory. The "saline and free" ammonia was measured by a simplified Wanklyn process. If we understand the author aright, there were several different waters or solutions in each cage, so that the numbers of eggs collected is a measure of the insects' preference. Gravid female *Anopheles* were introduced in considerable numbers, generally 20-30 per cage. The experiments were repeated a number of times and the results show clearly that (in cages) *A. culicifacies* will lay eggs freely in concentrations up to about 6 parts of free ammonia per million. The upper limit for *A. subpictus* is higher, and this species appears to avoid water with less than 1 part p.m. when other waters are available.

A few observations were made on the ammonia concentration of water in which larvae of these two species were found in nature, and the more extended work of SENIOR-WHITE is considered. It seems that in the field the upper limit for *A. culicifacies* is very much lower than in the laboratory. [We should be disposed to continue the cage experiments, using fewer females per cage (so as to exclude any possible

effect of overcrowding) ; a dish of distilled water in each cage would provide a good control. It would also be advantageous to study the distribution of the eggs of species of *Anopheles* in nature, if the prevalent species are capable of being identified by their eggs.]

P. A. Buxton.

HACKETT (L. W.) & MISSIROLI (A.). **The Varieties of *Anopheles maculipennis* and their Relation to the Distribution of Malaria in Europe.**—*Riv. di Malariologia*. Sez. I. 1935. Vol. 14. No. 1. pp. 45–109. With 4 plates. [66 refs.]

— & —. Les variétés d'*Anopheles maculipennis* et leur relation avec la distribution du paludisme en Europe.—*Medicina Paisés Cálidos*. Madrid. 1935. Jan. Vol. 8. No. 1. pp. 1–60. With 23 figs. [65 refs.]

This is an excellent review of the subject illustrated with tables, photographs and drawings, together with Appendices giving details of the methods of collecting eggs, examining them and sending them by post.

"It is now clear that *A. maculipennis* is not a homogeneous species, but a collection of widespread varieties." In 1920 ROUBAUD suggested that there were two races of *A. maculipennis*, one with many teeth which fed on animals, and another with few teeth, which fed on man. According to ROUBAUD, in regions with well-stabled cattle, competition favours the insects with strong dental armatures fitted for piercing the tough hides of animals, and so a zoophilic race becomes differentiated. Where such conditions do not exist, undifferentiated *maculipennis* remain and continue to bite man. An average maxillary index of 14–15 is an indication of differentiated zoophilism ; populations with an average maxillary index below 14 are malaria carriers.

FALLERONI was the first to give names to any of the varieties of *A. maculipennis* ; he noted, in 1924, that the eggs of the anopheles from the Pontine marshes were of two kinds, grey and dark. In 1927, he proposed the name "*messiae*" for the form with the dark, barred egg, and the name *labranchiae* for the form with the grey dappled egg. The *labranchiae* in the south had a lighter egg than those in the north. In the same year, van THIEL showed that the "short wings" and "long wings" of Holland were valid races, and gave the name *atroparvus* to the former. *Atroparvus* has been shown to be identical with the dark grey egged northern *labranchiae*, and therefore the latter name is now restricted to the southern variety with the lighter egg. The generally accepted varieties are :—

maculipennis, Meigen, or *typicus* ; egg with 2 simple bars.

messeae, Falleroni ; egg dark (barred).

melanoon, Hackett, ; egg uniformly black. Possibly a form of *messeae*.

atroparvus, van Thiel ; egg dark grey dappled.

labranchiae, Falleroni ; egg light grey dappled.

elutus, Edwards ; egg uniformly grey.

These varieties are identified by (a) the egg marking and the character of the floats ; (b) the larval hairs ; (c) the external harpaginal spine of the male adult. A table is given showing the morphological difference between the six varieties. The authors are of opinion that "the egg-types provide the only satisfactory method of dividing *A. maculipennis*

into a number of constituent forms, with a minimum of overlapping." Roubaud's maxillary index, and the wing-length classification of van Thiel have statistical value only; they are useless in the classification of individuals and have only a local validity, *i.e.*, the long wings in one country may be no longer than the short wings in another; the longest wings found in Italy are half a millimeter shorter than the shortest wings of North Europe. The number of teeth of *atroparvus* averages more than 17.5 in Germany and Holland, while it does not reach 16 in either *atroparvus* or *messiae* in Italy.

The subdivision of *A. maculipennis* into varieties on the ground of differences in the eggs is supported by biological differences in (a) the selection of breeding-places, (b) sexual behaviour, and (c) winter habits. *Atroparvus* breeds in saline water, *messiae* in fresh; *atroparvus* will copulate in a closed space ("stenogamy"), the other varieties will not; *atroparvus* does not go into complete hibernation, the other varieties do. The validity of the classification is further supported by (d) the constancy of the egg characters in a given variety; (e) the constancy of the morphological and biological characters of the adults bred from a given type of egg; and, finally, (f) "attempts to cross mate the different forms have so far revealed a barrier of sterility between them which is the strongest evidence of their specific nature."

The relation of the different varieties to malaria.—All the varieties of *A. maculipennis* are equally susceptible to malaria and, though some prefer to feed on animals, there is never an insurmountable barrier, either microclimatic or instinctive, between any of the varieties and man. In almost the whole of northern Europe *A. maculipennis* lives at the expense of domestic animals, and man is said to be protected from malaria through "deviation" of the anopheles by animals. In the malarious regions of southern Europe, *A. maculipennis* bites man persistently. The principal reason for the difference in its behaviour, in the north and the south, is that the anopheline population of the latter regions consists of varieties such as *elutus* and *labranchiae* which prefer to feed on man. For example, at Diamantina on the river Po, *elutus* occurs mixed with more northern races of *A. maculipennis*; 226 *elutus* were caught there in stables and 158 in houses; while, of the other races, 478 were caught in stables and only 3 in houses. BARBER and RICE found in Albania and Northern Greece that 50 per cent. of the *elutus* contained human blood, but only 6 per cent. of the *typicus* and *messiae* contained it. Again, they found 42 infected *elutus* for every single infected insect of the other varieties. It is probable that there is a profound cleavage between the barred-egg group (*typicus*, *messiae*, and *melanoon*) and the spotted-egg group (*atroparvus*, *labranchiae* and *elutus*) which favour saline water.

The races *typicus* and *melanoon* are rarely, if ever, associated with malaria.

The race *messiae* is effectively deviated by animals in summer and goes into complete hibernation in winter. It was associated with some outbreaks of benign tertian shortly after the war, and more recently in Rumania.

The race *atroparvus* is not dangerous as a rule, but slight variations in its environment can make it so. It is responsible for whatever malaria occurs in northern Europe. Much depends on the standard of living and the way people house themselves and their animals. The range of *atroparvus* is the whole coastline of northern Europe

from France, through Great Britain, Holland, Sweden, Denmark, Germany to Danzig and beyond ; but malaria is endemic only in the coastal area of Holland and a small contiguous zone of German East Friesland. Here the same variety of insect is prevalent all along the coast, and the difference must lie in the environmental circumstances which induce this mosquito to feed on man in one place, and on animals in another. Where *atroparvus* is present, war, indigence or squalor may bring malaria. In Holland, *atroparvus* feeds on animals during the summer, but it does not go into complete hibernation during the winter ; though it continues to feed it ceases to lay eggs, and is therefore not obliged to leave its shelter (gonotrophic dissociation). If an infected *atroparvus* shelters in a house it remains " fixed " there, and transmits the infections during the winter which are responsible for the spring epidemic of benign tertian in Holland. On the north coast of Germany, *atroparvus* is found in houses during the summer.

The races *labranchiae* and *elutus* are always associated with an intense malaria, and they try persistently to enter bedrooms even when there is an abundance of animals. They are the mosquitoes of the Mediterranean littoral.

The Geographical Distribution of the several Types.

Maculipennis.—This is the preponderating variety in Norway, and is found in almost pure culture in the Black Forest and Harz Mountains of Germany. It is not found in England.

Messiae.—This variety is probably numerous in all the fresh water regions of Europe. The most southern points of its range are Italy and the Balkans. It is found in Sweden, Denmark, Germany (the lakes of Holstein and Mecklenburg, the valleys of the Oder and Rhine, the Bavarian lakes), France, England, Northern Italy, the valley and delta of the Danube in Rumania.

Melanoon.—This closely related form is found in the rice fields of north Italy and north-eastern Spain.

Atroparvus.—This salt water breeder is found all along the northern coasts of Europe, Warnemünde on the Baltic, the marshes at the mouth of the Elbe, the low marshes of the Netherlands, the mouth of the Thames, Hayling Island. Inland, it is met with on salty soil ; for example : near Lübeck, near Bucharest, in the steppes. In some places, it is found breeding in fresh water : in Buckinghamshire, and near Hamburg.

Elutus.—This variety displaces *atroparvus* in the south, and is found along the Montenegrin and Dalmatian coasts, the Balkan Peninsula, Asia Minor, Syria, Palestine, Persia, North Africa.

Labranchiae.—This begins to take the place of *atroparvus* in the north of Italy and is the dominating variety in the Roman Campagna, the Pontine marshes and the west coast of Italy.

Atroparvus, *labranchiae* and *elutus* are the three varieties of *A. maculipennis* which are chiefly concerned with malaria. They lay spotted eggs, and they can breed in saline water. *Atroparvus* is the only race of *maculipennis* found breeding in cool, northern water of moderate salinity. *Labranchiae* prefers the same kind of breeding-place, namely brackish marshes along the coast ; but this variety is found in warmer waters, further south. *Elutus* occurs over a wider range than *labranchiae*, but in the same kind of breeding-place. It can breed in waters of higher salinity than *labranchiae*. It breeds in fresh water in Palestine.

W. F.

- i. EKBLOM (Tore). Les races suédoises de l'*Anopheles maculipennis* et leur rôle épidémiologique. [**The Swedish Races of *A. maculipennis* and their Rôle in Epidemiology.**—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 284–289. With 2 figs. (1 map).]
- ii. SERGENT (Et.). Au sujet des variétés de l'*Anopheles maculipennis* du groupe *labranchiae*. [**The Varieties of *A. maculipennis* of the *labranchiae* Group.**—*Ibid.* p. 290. With 1 plate.]

i. Although in Sweden malaria is now only sporadic, and the attacks diagnosed as such are generally of foreign origin, indigenous but very rare cases occasionally occur, forming a striking contrast to great epidemics of the past, which at certain times involved a large portion of the country. Thanks to BERGMAN (1877), we possess exact knowledge of the local distribution of the malady in the middle of last century.

Relying on egg-characters, the validity of which has been disputed by ROUBAUD and GASCHEN (see this *Bulletin*, Vol. 30. p. 611), the author finds that, in addition to typical *A. maculipennis*, the races *messeae* and *labranchiae* occur in Sweden as in Italy and Holland. While *messeae* is generally distributed throughout the anopheline area, the other two races are of less regular occurrence, and *labranchiae* appears to be mainly confined to the south coast; on the west coast it is replaced by *messeae* and *typicus*, and on the east coast by *messeae*. North of the line Kalmar-Kungsbacka the two last-mentioned races alone are found. In the interior the typical race preponderates.

A comparative study of the distribution in Sweden of the three races of *A. maculipennis* mentioned above, and of the bygone occurrence of malaria, both epidemic and endemic, shows that :—

- (i) *labranchiae* is absent from most of the quondam malarious regions ;
- (ii) *typicus* predominates in those parts of the country where malaria was formerly epidemic as well as endemic ;
- (iii) round Stockholm, where in 1927 there were a few sporadic and apparently indigenous cases of malaria, the local races of *A. maculipennis* are *messeae* and *typicus*, which, as vectors, have previously been considered of less importance than *labranchiae*.

It is not absolutely certain that the Swedish races of *A. maculipennis* are identical with, e.g., those found in Holland.

ii. In the vicinity of Algiers, 90 per cent. of female *A. maculipennis* lay eggs of pure *labranchiae* type ; the eggs of the remaining 10 per cent. exhibit characters intermediate between those of the eggs of the latter and those of the eggs of ROUBAUD's recently described var. *sicaulthi* (see p. 814 below).

A brief addendum by ROUBAUD admits that the eggs figured by the author as deposited by his "remaining 10 per cent." are very similar to, if not identical with, those of var. *sicaulthi*. It would be interesting, by means of a study of selected broods, to determine the race and geographical distribution in Algeria of *Anopheles* laying indistinctly speckled eggs.

E. E. Austen.

SERGENT (Et.) & TRENSZ (F.). Premières études sur les races d'*Anopheles maculipennis* en France et en Algérie (1933). [**The Races of *A. maculipennis* found in France and in Algeria, in 1933.**—*Arch. Inst. Pasteur d'Algérie.* 1935. Mar. Vol. 13. No. 1. pp. 1–10. With 6 figs. on 1 plate.]

The only race of *A. maculipennis* hitherto met with by the authors in Algeria (three localities) is *labranchiae*, which is indifferently zoophile,

since the adults bite man and domestic animals alike ; and, whether they feed upon human or animal blood, the maxillary index (14 to 15 on the average) is the same. It does not appear that the Algerian *labranchiae* has become less dangerous in the localities studied, where the insects have long found conditions favourable to the development of zoophily.

As regards France, at Moustolat, a village in the Limousin (Corrèze), malaria disappeared more than fifty years ago. The dappled *Anopheles* eggs found and examined there in the summer of 1933 have smooth and transparent floats like cellophane, whereas those on Algerian eggs are wrinkled and finely striated ; the Moustolat eggs are also narrower than the Algerian, and of a slightly yellowish grey. Instead, therefore, of also belonging to the *labranchiae* race as was at first supposed (see this *Bulletin*, Vol. 30, pp. 611-612), the Moustolat *Anopheles* are really *atoparvus*, and the local existence of this zoophile race, of which the maxillary index was found to be between 16 and 17, is in accord with the present absence of malaria. Two batches of eggs belonging to *A. maculipennis typicus* were also found.

In Alsace, where anophelism is still intense though the inhabitants are not molested, 206 out of 208 batches of eggs examined were found to belong to the race *messeae*, albeit more or less important variations were noted in the general colour of the egg and in the degree of wrinkling of the floats ; in the great majority of the batches (180 out of 208) the floats were strongly wrinkled. A single batch of eggs was entirely black (= race *melanoon*). E. E. A.

GALLIARD (Henri). Contribution à l'étude des races d'*Anopheles maculipennis* en Tunisie. [**The Races of *Anopheles maculipennis* in Tunis.**—*Arch. Inst. Pasteur de Tunis*. 1935. Apr. Vol. 24. No. 2. pp. 343-351. With 3 figs. [15 refs.]

After a preliminary discussion and characterization of the races or varieties of *A. maculipennis* in general, the author proceeds to consider larvae collected by him in certain specified localities in Tunis. All belonged to var. *labranchiae*, as did also some thirty batches of eggs, though one batch of entirely black eggs resembled those of var. *melanoon*. Thus in Tunis, as in Algeria, the predominant and perhaps the only race of *A. maculipennis* is var. *labranchiae*. It is certain, however, that *A. elutus* must exist in the coastal region, and this species may also breed in brackish water in the Sahel.

On the other hand, in North Africa, the absence or recession of malaria in a given region must be explicable otherwise than by the distribution of the different races of *A. maculipennis*. The author, in conjunction with SAUTET, has already demonstrated, in Algeria, the exclusive presence of var. *labranchiae* in two regions, in one of which malaria is disappearing, while in the other it is still extremely severe ; and similar conditions have been found by the same investigators in Corsica, where the distribution of the endemic is very irregular, although the anopheline fauna is everywhere the same. It may perhaps eventually be found that var. *labranchiae* in Corsica and North Africa, although so similar morphologically to the same variety in Continental Europe, possesses biological characters which are entirely different.

E. E. A.

ROUBAUD (E.). Variété nouvelle de l'*Anopheles maculipennis* au Maroc, *A. maculipennis sicaulti* (n. var.). [**A New Variety of *Anopheles maculipennis* found in Morocco, *A. maculipennis sicaulti*, var. nov.**].—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 107–111. With 7 figs. on 2 plates & 1 text fig.

At his insectary in Paris the author received living females from an *A. maculipennis* population, which SICAULT had been studying for several years in the region of Rabat, Morocco. The deposition of batches of eggs by these insects, followed by the rearing of a new generation of adults, furnished morphological and biological data showing that the Moroccan individuals represent yet another new race, allied to *labranchiae* and here described under the name given above.

The egg, which has a dusky hue, is blunter at each end than that of *labranchiae*, and, though becoming progressively darker towards the poles, is without the sharply defined dark caps exhibited by the egg of the race in question; the markings on the middle region, which appears paler in certain lights, are also much less numerous and less sharply defined. In the larva, the branches of the hair on the second abdominal segment are filiform instead of palmate.

In the adult, the white spot in the fringe at the tip of the wing is generally narrower than in *labranchiae*, and scarcely so large as the interval between the end of the anterior branch of the first alar fork and the third longitudinal vein: all the harpagonal spines in the male hypopygium are sharp.

Biologically the new variety is closely allied to *labranchiae*. It is eurygamous (*i.e.*, will not mate in a confined space) and homodynamous, ovipositing in winter at a medium temperature; it is also paucidentate, with a maxillary index of about 13.7, and by predilection androphile rather than zoophile.

E. E. Austen.

RIVERA (Julio) & HILL (Rolla B.). Persistencia de los caracteres diferenciales de los huevos, larvas y adultos, en diferentes generaciones de *Anopheles maculipennis (atroparvus)*. [**Persistence of Differential Characters in Eggs, Larvae and Adults of Different Generations of *A. maculipennis*.**].—*Medicina Paises Cálidos*. Madrid. 1935. July. Vol. 8. No. 7. pp. 313–319. [13 refs.] English summary (7 lines).

Authors' summary:—

"From May to October six generations of *A. maculipennis* var. *atroparvus* were raised, beginning with a single fertilized female. Egg, fourth stage larva, and male and female characters were studied in each generation. Each generation bred true to type for differential characters. Slight variations were noted particularly in size of eggs, and float, wing length, maxillary index and duration of developmental stages, which we attribute to environmental influence."

HILL (Rolla B.), OLAVARRIA (Jose) & RIVERA (Julio). Longitud de vuelo del *A. maculipennis (atroparvus)*. [**Length of Flight of *A. maculipennis (atroparvus)*.**].—*Medicina Paises Cálidos*. Madrid. 1935. June. Vol. 8. No. 6. pp. 265–268. English summary (5 lines).

"In various experiments with stained *A. maculipennis* var. *atroparvus* to test the length of flight it was found that a certain number will fly from 4 to 5½ kms. in 18 to 36 hours, apparently in search of food. The number found is sufficient to account for the presence of anopheles in the center of a protected zone of 4 kms. radius."

OLAVARRIA (Jose) & HILL (Rolla B.). Algunos datos sobre las preferencias hemáticas de los *A. maculipennis*. [**Blood Preferences of *A. maculipennis*.**]—*Medicina Paises Cálidos*. Madrid. 1935. Apr. Vol. 8. No. 4. pp. 169-176. [11 refs.] English summary (7 lines).

Summary :—

"The results of 2,500 precipitation tests performed on bloods from freshly engorged *A. maculipennis* var. *atroparvus* caught in houses and in stables [in Cáceres, Spain] are given, together with the technique of the reactions.

"Approximately 40 per 100 of those caught in houses and 2 per 100 of stable-caught mosquitoes had human blood. Since less than 7 per 100 of the total anopheles production is caught in houses, it follows that a maximum of 5 per 100 feed on human beings one or more times."

A. G. B.

FACCIOLI (Domenico). Sulle varietà di *Anopheles maculipennis* presenti nella piana di S. Eufemia (Calabria). [**Varieties of *A. maculipennis* in the Calabrian Plain.**]—*Riv. di Malariologia*. Sez. I. 1935. Vol. 14. No. 2. pp. 167-184. With 1 fig. English summary (9 lines).

"In Calabria—Piana di S. Eufemia—four varieties of *A. maculipennis* (that is: *labbranchiae*, *maculipennis*, *messeae*, *elutus*) are found. The *labbranchiae* variety predominates and is the dangerous vector of malaria. All the varieties of *A. maculipennis* are found more frequently associated with animals than with man. The commonest egg type of *labbranchiae* is somewhat different from that we observe in other regions. The greatest number of ovipositions is given by the anopheles caught in the stables; the zoophile and anthropophile anopheline races show their highest or lowest percentage of oviposition " in different months of the year.

H. H. S.

KHARITONOV (D. E.). **Observations on the Biology of the Malaria Mosquito (*Anopheles maculipennis* Meig.) in the Manchazh Subdistrict of the Ural Province.**—*Bull. Inst. Rech. Biol. Perm.* 1934. Vol. 9. No. 6-8. pp. 297-309. [10 refs.] [In Russian.] [Summarized in *Rev. Applied Entom.* Ser. B. 1934. Dec. Vol. 22. Pt. 12. p. 239.]

"A detailed account is given of observations on the adults of *Anopheles maculipennis*, Mg., carried out in the spring and summer of 1925 in the south-west of the Ural Province. In most of this area there were apparently three generations in the year, the adult males occurring in mid-June, mid-July and early August; but in one locality, where streams, etc., dried up by the middle of July, there were only two generations. Females with developed fat-bodies were first observed in the second half of July and became very abundant during August. Of the females found hibernating in April, 90 per cent. were in warm sheds for cattle, pigs and sheep; of the other types of shelters, basements of unheated buildings were preferred, and only a few mosquitos were taken in basements and rooms of inhabited houses. Some occurred in suitable quarters at a distance of nearly a mile from water and at a level of about 100 ft. above the ground. They chiefly congregated on ceilings and the upper parts of walls, especially in corners. They seldom assumed the typical Anopheline resting position, usually resting in the same way as *Culex* does. Badly built animal quarters with large cracks in the walls were avoided. Activity was resumed about mid-April, and active oviposition apparently occurs in the field in the first half of May. In the second half of April, females oviposited in the laboratory within 4½-8½ days after a blood meal, and females taken in hibernation quarters at the end of the month and containing fresh blood did so in about 3 days. The number of eggs laid varied

from 89 to 248. In the summer, most of the mosquitos occurred by day in warm sheds for domestic animals, and only a few in dwellings and outhouses."

HOFFMANN (Carlos C.). La formación de razas en los Anopheles Mexicanos. I. *A. maculipennis* y *A. quadrimaculatus* y una raza nueva del *maculipennis*. [The Formation of Races in Mexican Anopheles. I. *A. maculipennis*, *A. quadrimaculatus* and a New Race of the Former.]—*An. d. Inst. Biol.* 1935. Vol. 6. No. 1. pp. 3-22. With 20 figs. [31 refs.] German summary.

A. quadrimaculatus, found in Mexico in a form indistinguishable from that which occurs in Southern U.S.A., is a denizen of the Gulf coast, and does not penetrate far inland. Statements by previous writers, as to its occurrence in the uplands and mountain valleys of the interior, in reality refer not to this species but to a new race or form of *A. maculipennis*, of which, in its various stages, a detailed description is given in this paper under the name *A. maculipennis aztecus*. The egg is described as light brown, without spots; the floats occupy roughly 40 per cent. of the total length, and have 25 ribs and a finely granular intercostal membrane.

At an altitude of upwards of 7,000 feet (2,250 metres), *A. m. aztecus* occurs throughout the year. During winter, when the males disappear, the females are found in houses; larvae in all stages are to be met with at any time, and even survive being frozen over for a brief period. Breeding takes place by preference in ditches, containing clean water well supplied with algae and protozoa; rearing in the laboratory presents no difficulty.

F. E. A.

EJERCITO (Antonio). Biological Control of Anopheline Vectors of Malaria in the Philippines: Preliminary Report.—*Jl. Philippine Islands Med. Assoc.* 1935. Apr. Vol. 15. No. 4. pp. 177-194. With 4 figs.

The experimental damming and flushing of a stream reduced the number of *A. minimus*.

A series of dams provided with gates was constructed in a stream, dividing it into six sections. The stream was flushed at intervals by opening the gates and setting free the imprisoned water. The average number of *A. minimus* (the principal carrier), per dip, taken before the damming of the stream, was 2.45. The average, per dip, after "the stream had been disturbed by flushing now and then," was 0.73 per dip. *A. maculatus*, which is normally an "accidental or seasonal breeder," bred in the dammed up water and was found in the lower parts of the stream after flushing, although there was none there before. Cutting down the shade along the sides of streams is recommended because observations have shown that while *A. minimus* var. *flavirostris* could be found in the shady reaches of the stream, none was present in the portions where the shade had been cleared away.

W. F.

SINTON (J. A.) & MAJID (Syed Abdul). The Dispersion of Anopheline Larvae by the Flow of Streams, and the Effect of Larvicides in preventing this.—*Records of the Malaria Survey of India.* 1935. Mar. Vol. 5. No. 1. pp. 3-17.

Larvae which drifted into a controlled area in the intervals between the applications of Paris green were not destroyed (see AMBIALET, p. 134 above).

A slowly moving stream was treated regularly with Paris green ; but in spite of this numerous large anopheline larvae and pupae could be found in it on the next day after each dusting. It was suspected that they had drifted in from the upper reaches. In order to investigate this, a net or barrier made of muslin was stretched across the stream, with about 10 inches of its width above the surface of the water and 10 inches below. The muslin strained off the material floating down the stream, and this was collected and examined. The result showed that in this stream, which flowed at the rate of 300 yards an hour, about a thousand larvae and pupae drifted into the controlled area every hour. Though the Paris green dusted in the controlled area had an excellent immediate effect, it soon drifted away and sank ; consequently it had no effect upon the larvae which drifted into the area during the 5 days' interval between the dustings. The continuous application of oil, made by means of oil-balls, greatly diminished the number of larvae which drifted into the controlled area.

W. F.

TILLI (Pietro). Esperimenti pratici di disanofelizzazione idrica nell'Agro Romano mediante la calciocianamide. [**Practical Experiments with Calcium Cyanamide as a Larvicide.**]*—Riv. di Malariologia.* Sez. I. 1935. Vol. 14. No. 2. pp. 192-200. French summary.

The author's previous tests with calcium cyanamide (nitroline) as a larvicide have been referred to [see this *Bulletin*, Vol. 31, p. 189]. In the present article he gives an account of further experimental work in the field using new road-dust as a diluent and in strengths from 10 to 50 per cent. applied every 8, 15, or 20 days. It acts best in a strength of half and half, at which it kills anopheles and culex. It is destructive to the plankton on which the larvae feed. The compound, however, has drawbacks. It causes a high mortality among *Gambusia* and therefore cannot be employed in waters where fish are preserved ; it also arrests vegetation ; it sets up conjunctivitis and dermatitis in those working with it unless glasses and gloves are worn and it is well to use long tubes for projecting the mixture.

Although the author mentions the destructive action of the cyanamide on vegetation he recommends its use in rural districts " because it possesses at the same time larvicide and fertilizing properties " and is more economical than Paris green [but the latter is used in a strength of only 1 per cent., whereas the cyanamide needs to be 50 per cent. of the mixture with dust].

H. H. S.

DE BENEDETTI (Augusto). Outillage mécanique pour la préparation d'une poussière flottante selon le procédé de Benedetti appliqué par le service de délarvisation de la ville de Milan. [**Benedetti's Apparatus for preparing a Floating Powder.**]*—Rev. d'Hyg. et de Méd. Préventive.* 1935. Apr. Vol. 57. No. 4. pp. 267-273. With 3 figs.

Road dust is no longer obtainable, because the roads are tarred. Ordinary garden soil cannot be used for mixing with Paris green because it sinks at once, but the author has devised a method of mixing it with oil and then heating it, which gets over the difficulty. After the earth has been mixed with the oil, it is heated to 250°C. in one of the portable furnaces used for melting pitch and, after being mixed with Paris green, it is distributed by a blower devised by the author. Figures showing the apparatus are given.

W. F.

SATYANARAYANA (K.). **Anti-Malarial Operations in the Vizagapatam Harbour Construction Area (1927-1933).**—*Records of the Malaria Survey of India*. 1934. Dec. Vol. 4. No. 4. pp. 343-362. With 2 maps & 5 graphs.

This describes "oil-balls" for using in streams.

Vizagapatam has always been a malarious locality and when the construction of the harbour was begun in 1926 it was feared that there might be a great increase in the disease. The Harbour Authorities consequently decided to take steps to prevent such an occurrence, and they have succeeded not only in maintaining a healthy labour force engaged on the work of construction, but also in preventing an outbreak of malaria in the city while the work was in progress. Some of the control operations were radical and costly. For example, the malarious inhabitants of 4 villages who were a dangerous source of infection to the labour force of the harbour were transplanted to a safer distance, and a tunnel 1,400 feet long was driven through a hill at a cost of 70,000 rupees in order to divert a stream. About 169 wells were filled up, much jungle and prickly pear was cleared away; streams were canalized and drains were cut, oil and Paris green were used; a mixture of carbolic acid, kerosene and petrol was used as a spray; fishing and grazing rights were restricted; wet cultivation in the neighbourhood of the harbour works was prohibited. "Four Oaks" sprayers were used for most of the oiling, and, in addition, oil balls were employed. These were made by stitching up a mixed mass of waste cotton, Indian corn-cobs and sawdust in gunny bags. They were about the size of a football and weighed 4 to 5 pounds. They were soaked in oil for 24 hours, during which time they absorbed about 3 pounds. They were then tethered in streams where they made a good film for about a week.

W. F.

JAMES (J. F.). **Fumigation and Trapping of Mosquitoes.**—*Indian Med. Gaz.* 1935. Mar. Vol. 70. No. 3. pp. 143-144. With 1 fig.

The author trapped about 15,000 anopheles in barracks during a period of 11 weeks. Mosquitoes fly towards any lighted exit when a fumigant is burnt. The method adopted was to fix a diaphragm of black cloth over one of the windows of the barracks. In the middle of the black cloth was a hole about 8 inches in diameter. The mouth of a thin muslin bag about 6 feet long was fastened round the edges of this hole, and the blind end of the bag was attached to some object outside the window. All the other windows and the doors were closed, and a coil of a proprietary fumigant burnt. After half an hour the mouth of the bag was tied up, the bag removed, and the contents killed by chloroform.

W. F.

SERGIEV (P. G.). Sur l'importance épidémiologique de la destruction des moustiques dans l'habitation. [**The Importance of destroying Mosquitoes in Houses.**]—*Med. Parasit. & Parasitic Dis.* Moscow. 1934. Vol. 3. No. 4. pp. 315-322. [10 refs.] [In Russian. French summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. p. 76.]

"The author considers that Anophelines in houses should be destroyed in the spring and summer rather than in winter, since most of

them hibernate elsewhere. Moreover, malaria sporozoites are rapidly killed at temperatures near freezing point and do not survive the winter in mosquitos that have become infected in autumn. On resuming activity in the spring, the surviving mosquitos, including those from unknown or remote hibernation quarters, concentrate in inhabited houses, stables and cattle sheds, and should be destroyed from this time onward, but particularly in July, August and September when the rate of infection in them reaches its maximum. In the central part of the northern Caucasus in August 1933 and in Daghestan in August and September 1932, the infection index of mosquitos in houses was as high as 13.5, and 11.36 and 23.58 per cent., respectively."

RUIBINSKIĭ (S. V.) & LEVIT (M. S.). Die Fischzucht als Bekämpfungsmittel der Malaria in der Ukraine. [**Fish-breeding as a Method of controlling Malaria in the Ukraine.**]*—Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 2. pp. 151–159. [27 refs.] [In Russian. German summary.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Mar. Vol. 23. Pt. 3. p. 86.]

"In the Ukraine, most of the endemic centres of malaria occur in districts with vast expanses of water resulting from river floods. Neglected mill-ponds also offer favourable breeding-places for mosquitos, of which *Anopheles maculipennis*, Mg., is the chief vector of the disease. As it is planned to use large accumulations of water for breeding fish, investigations were carried out in 1932 on the possibility of rendering the fish-ponds unsuitable for mosquito larvae or using the fish against them. For this purpose, over 50 carp-ponds were examined near Kiev. Measures suggested to prevent the breeding of Anophelines include the removal from the water of vegetation, thus depriving the larvae of shelter from the fish, the improvement of the channels by which the ponds are filled or drained and in which Anopheline larvae are often numerous, dusting with Paris green, which, unlike oil, does not affect the fish, and stocking the ponds with young carp, which feed readily on the larvae. The value of other fish in this respect is discussed, and the introduction of *Gambusia* is particularly advocated, as experiments have shown that it can be established in the Ukraine. When a pond is constructed, the bottom should be made very smooth so that it can be thoroughly dried when the pond is drained."

SICAULT (G.) & ROULE (S.). Note sur la biologie du *Gambusia Hoolbrocki* [sic] au Maroc. [**Biology of *G. holbrooki* in Morocco.**]*—Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 134–141.

The multiplication and activities of *Gambusia* were studied in a swamp 50 by 1 to 4 km. in area connected with two rivers; *Anopheles* abounded.

An attempt made to drain the swamp by means of a canal proved ineffective and *gambusia* were introduced. Their fecundity was surprising. In 7 months they stocked an area of 10,000 hectares. Where they were in sufficient concentration in warm weather (at least 20 per sq. metre) they prevented all anopheline increase. In the autumn and even in the spring when the temperature is below 5°C. the fish leave the shallow water for the deeper pools. Larvae can develop at such temperatures; at these times therefore the usual antilarval measures may be employed.

A. G. B.

BARBOSA (Amando) & ARJONA (Benito López). **El paludismo en el primer año de la vida.**

This book is reviewed on p. 837.

BRITISH MEDICAL JOURNAL. 1935. Mar. 23. p. 590.—**The Malaria Epidemic in Ceylon. First-Hand Experiences.**

In the summary of Dr. V. B. WIGGLESWORTH's lecture on the Malaria Epidemic in Ceylon (p. 732 above), he was reported as having said that to have prevented the breeding of *A. culicifacies* over the affected area would have been a far vaster undertaking than anything so far attempted for the control of malaria. This was misleading: what he really said was, "for the control of *rural* malaria." W. F.

CIANCAS RODRIGUEZ (Ramiro). Mi experiencia en el tratamiento del paludismo.—*Medicina Paises Cálidos*. Madrid. 1935. Aug. Vol. 8. No. 8. pp. 385–398.

MONNEROT-DUMAINE. Paludisme chez un enfant diabétique. Acidose grave.—*Rev. Méd. et Hyg. Trop.* 1934. Nov.–Dec. Vol. 26. No. 6. pp. 268–271. With 1 chart.

MORIN (Henry G. S.) & CARTON (P.). De l'influence des facteurs climatiques sur la répartition de l'endémie palustre en Indochine.—*Rev. d'Hyg. et de Méd. Préventive*. 1935. Apr. Vol. 57. No. 4. pp. 262–266.

NOVET (D.), BENOIT (G.) & ATMANN (R.). Action thérapeutique de quinoléines à poids moléculaire élevé, homologues de la plasmoquine, sur les hématozoaires des calfats et des serins.—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 729–730. [See this *Bulletin*, ante, p. 117, where, however, the names are spelt differently.]

BLACKWATER FEVER.

PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE. 1935. Apr.
Vol. 28. No. 6. pp. 671-680 (Sect. Comp. Med. pp. 21-30.
[17 refs.] **Discussion on Haemoglobinuria** [BARCROFT (J.),
MINETT (F. C.), MACKIE (F. P.), SCORGIE (N. J.), CHRISTOPHERS
(Rickard), WEBER (F. Parker), EDWARDS (J. T.)].

Barcroft in opening the debate said that any discussion on haemoglobinuria held in the first decade of this century would, he felt sure, have entailed a discussion of the function of Bowman's capsule and of the rôle played by the glomerular covering. Lately, opinion has crystallized in the direction of the view that Bowman's capsule is simply a filter. Permeability of this filter has been investigated by BAYLISS, KERRIDGE and RUSSELL, who found that of the materials which they tested those with molecular weights of less than 70,000 passed through the membrane and appeared in the urine, whilst those with higher molecular weights were retained in the blood. This is about the molecular weight of haemoglobin, which is consequently just on the border line as regards excretion; sometimes it will pass through and not at other times.

The question arises whether all haemoglobin molecules are of the same weight, or whether 68,000 is a sort of average weight. The weight which corresponds to one atom of iron is 17,000; the complete molecule therefore contains four such units. It might be that all the molecules were uniform and contained four units; or it might be that the units are loosely attached, in twins, triplets, quadruplets, quintuplets, and so on, but on the average, quadruplets. The matter had been investigated by ADAIR, who decided in favour of the uniformity of the haemoglobin molecules. The molecules of haemoglobin in the red corpuscle appear uniformly to have a molecular weight of 68,000.

Barcroft then passes to the consideration whether haemoglobin found elsewhere than in the corpuscles differs from corpuscular haemoglobin. Within the last year or so the constitution of the pigment in muscle has been investigated, and it appears that myohaemoglobin is not the same as the pigment in blood. Among other differences it has a low molecular weight, and consequently if liberated in the plasma should appear with greater readiness in the urine than does corpuscular haemoglobin. As the spectra of the two forms of haemoglobin are different there should be no difficulty in distinguishing between them in urine, assuming they retain their native properties.

Minett gave a brief summary of the haemoglobinurias and myoglobinurias in animals. He classifies them as follows:—

"Haemoglobinurias.

"(1) Due to destruction of erythrocytes by parasites or their products, e.g. certain protozoa, bacterial haemolysins.

"(2) Due to lowered resistance of erythrocytes.

"(3) Of doubtful or unknown origin, e.g. puerperal haemoglobinuria of cows, acute enzootic haemoglobinuria and jaundice in sheep.

"(4) Arising from miscellaneous causes, e.g. certain defined chemical agents, extensive skin burning.

"Myoglobinurias.

"Arising from 'destruction' of voluntary muscle: Paralytic myoglobinuria of horses (so-called 'equine haemoglobinuria'). Enzootic myoglo-

binuria of horses (so-called 'equine enzootic haemoglobinuria'). Myoglobinuria of cattle."

Mackie, Scorgie, Christophers and others continued the discussion.

W. Yorke.

STEUDEL (Emil). Schwarzwasserfieber und Chinin. [**Blackwater Fever and Quinine.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. July. Vol. 39. No. 7. pp. 277-287. [11 refs.]

Steudel says that whilst engaged in the production of a new work he had occasion to look through his old monograph entitled "Die perniziöse malaria in Deutsch-Ostafrika" published in 1894, and for the first time he reached a clear conception, chiefly on statistical grounds, of the relationship between blackwater fever and quinine.

Between 1891 and 1893 he treated 18 cases of blackwater, and being firmly convinced that this disease was a form of severe malaria he treated his patients with large doses of quinine, 3 to 5 gm. daily up to a total of 10 gm. The results were excellent; only three (16.6 per cent.) died, and of these two came to him before he adopted this particular line of treatment, and the third took ill when on a journey and was admitted to hospital only a few hours before death.

In 1895, F. PLEHN drew attention to the fact that blackwater usually followed the administration of quinine, and KOCH in 1897 put forward the theory that blackwater was not due to malaria, because in more than half of the cases malarial parasites could not be found. These observations, and others which followed, caused physicians to withhold quinine in this disease. In a table, Steudel gives the death rate from blackwater in German East Africa during the 10 years 1903-1912. In all 670 patients suffered from the disease and 125 (18.66 per cent.) died. Another table gives the European population and the number of deaths from blackwater during the same 10 years; in the first 3 years of the period 5.7 per 1,000 per annum of the population died of blackwater, and in the last 3 years 3.0 per 1,000 per annum died of this disease. During the 10 years in question the European population increased four-fold, whilst the number of cases of blackwater increased hardly two-fold. Apparently, therefore, one can conclude that not only the number of deaths decreased, but also that the relative number of cases of the disease decreased very materially. During the 6 years, 1927 to 1932, the English records show that there were 463 cases of blackwater and 118 (25.5 per cent.) deaths.

Steudel asks how it comes that about 40 years ago he had only 16.6 per cent. of deaths, whilst in much later times the death rate appears to have increased. He states that there are two main causes of death in blackwater, viz., anaemia and anuria; and the latter appears to be the commoner in German East Africa. He adds that it is curious that he never encountered anuria amongst his 18 cases; in fact he knows of the condition only from reading. He attributes the fact that none of his 18 cases developed anuria to the large doses of quinine which they received. Steudel believes that the quinine prevented the coagulation (Gerinnung) in the renal tubules and thereby prevented suppression of urine, and consequently lowered his death rate.

Quinine, however, increases blood destruction and thus increases the danger of anaemia. If this theory be correct, it is necessary to

seek for new drugs which will prevent the coagulation of haemoglobin in the renal tubules and which will not increase blood destruction.

W. Y.

AMY (A. C.). **Haemoglobinuria on the Indian Frontier. A Second Communication.**—*Jl. Roy. Army Med. Corps.* 1935. Feb. Vol. 64. No. 2. pp. 110–113.

This paper is really a continuation of those published last year and already summarized in this *Bulletin* [*ante*, p. 202]. The author describes another case of haemoglobinuria which ended fatally. This is the first to be reported since August 13, 1933. The patient was an Indian; the total amount of plasmochin administered was 0.06 gm., spread evenly over 3 days; the illness was rapid and severe; and stoppage of the drug immediately after it became evident that something was amiss produced not the slightest effect on the progress of the disease.

The author is still exercising himself on the question whether true blackwater fever occurs amongst natives in the north and north-west of India, or whether these cases are simply and solely due to plasmochin poisoning. He states that, unfortunately, the present case does not help him to solve this problem.

W. Y.

CHARTERS (A. D.). **A Clinical Study of the Spleen in Blackwater Fever.**—*Jl. Trop. Med. & Hyg.* 1935. Jan. 1. Vol. 38. No. 1. pp. 1–9. [23 refs.]

Clinical notes are given of 15 cases of blackwater fever amongst Indians living in Uganda, and as a result of his observations the author draws certain conclusions regarding the significance of the spleen in blackwater fever.

In 13 of the cases the spleen extended at least two fingers below the costal margin at the beginning of the attack, and it was noticed that a well-marked reduction occurred during the course of the disease. In the author's opinion the severity was proportional both to the degree and the rapidity of contraction of the spleen. Palpable spleens amongst Indian children in Uganda were not found below the age of one, and very large spleens not until after the age of two. Similarly, Indians with less than one year's residence in Uganda did not exhibit palpable spleens, and very large spleens were found only amongst those with over two years' residence.

The author concludes from this that it takes two years for a baby constantly infected with malaria to develop a spleen of over 3 fingers, and approximately the same period for an Indian who has not been in the district before to develop a spleen of similar size. Of 18 Indian patients who developed blackwater fever, 4 had been in Uganda 1 to 2 years, 4 from 2 to 4 years, and 10 for over 4 years. The absence of cases in the first year is to be associated with the rarity of an enlarged spleen.

It has been frequently stated that one attack of blackwater predisposes to another. Charters, however, believes that this is only the case when the first attack has been an incomplete one, *i.e.*, if the spleen has not undergone full contraction. In such cases the first attack is usually a mild one. On the other hand, if the spleen contracts to such an extent as to become impalpable, the patient seems to develop a prolonged immunity. An attack associated with this complete contraction

is usually of a severe nature. Examples are given in support of these contentions.

In dealing with the question of prognosis, Charters lays stress on the degree of rapidity of the contraction of the spleen. If contraction of the spleen is the main factor in the causation of blackwater fever, it is obvious that the greater the degree of contraction the more severe the attack. The study of the author's records shows that the small spleen was, as a rule, associated with a mild attack. Where the spleen is large the prognosis is not so simple. If there is complete contraction from a spleen of over 3 fingers to one that is not palpable, the disease is invariably very severe. For some reason or other it may suddenly stop contracting, and this phenomenon is accompanied by an immediate cessation of haemoglobinuria. The more rapid the contraction of the spleen, the more acute is the course of the disease. A large spleen which undergoes a very rapid contraction may result in a fatal termination before it has disappeared beneath the costal margin; and the very rapid contraction of even a small spleen may suffice to produce a fatal attack of blackwater.

Charters considers that a tender spleen is in an irritable condition and liable at any moment to contract and bring on an attack of blackwater, especially if there is an exciting cause such as a dose of quinine.

As a result of all this, the author believes that the best method of prevention of blackwater, apart from general malarial prophylaxis, is to impress upon the people the importance of regular medical examination, and in any case where the spleen is found enlarged to cause a gradual contraction of the organ by quinine administration. He adds "Should cases prove resistant to quinine, splenectomy will be a certain preventative."

W. Y.

CASTILLON (L.). Fièvre bilieuse hémoglobinurique, considérations thérapeutiques et pathogéniques. [*Therapeutic and Pathogenic Considerations on Blackwater Fever.*—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 199-207.]

Two cases of blackwater fever were examined with considerable care and a number of observations made on each; these are given in detail. These cases, which ran very similar courses, exhibited certain unfavourable signs, *e.g.*, hepato-renal deficiency, lowering of the cholestaemia, pronounced anaemia and very poor general condition; favourable signs were:—no diminution in red cell resistance, and passage of more than 500 cc. of urine daily, for "un bilieux qui pisse est un bilieux qui guérit, quelle que soit, par ailleurs, l'importance de son hémoglobinurie." [This seems sound common sense.]

In the author's opinion the cases exhibited certain points of interest from the point of view of therapy and also from that of pathogenesis. To the ordinary methods of treatment the author added subcutaneous injections of chlorhydrate of choline 2 cgm. daily. The blood cholesterol is diminished in malaria and may fall to 0.6 per 1,000. The author states that the action of choline in causing a rise in the cholestaemia is certain; in his second case it rose to 1.65 per 1,000, which is definitely beyond the normal level.

It is generally recognized that there are two causes which precipitate an attack of blackwater in a malaria subject, *viz.*:—quinine and exposure to cold. Quinine was no doubt the exciting cause of the paroxysm in the second of these two cases. In the first case, however,

neither of these two factors could explain the relapse of blackwater which occurred when the patient was in hospital under the most careful observation. The author suggests that a simple malarial paroxysm with a rise of temperature to 40°–41.5°C. sufficed in this case to upset the physico-chemical equilibrium of the blood. W. Y.

BAMFORD (C. B.). Observations on Therapeutic Malaria with Special Reference to a Case of Haemoglobinuria.—*Brit. Med. J.* 1934. Oct. 27. pp. 764–765. With 1 chart.

An account is given of a general paralytic, who developed haemoglobinuria following the treatment of his nervous condition by quartan malaria. The strain employed had passed previously through two patients who did not manifest any unusual symptoms. Another patient inoculated simultaneously with the same blood as the case under consideration manifested nothing unusual. When the patient had had ten paroxysms at daily intervals he was put on the usual course of quinine treatment, *i.e.*, 10 grains three times daily. Twenty-four hours later (after he had received 5 doses of quinine) he had a very severe rigor. Quinine was continued, however, and two days later the temperature rose again to 99.6°F. The skin exhibited an icteric tinge and the urine was observed to be unusually dark in colour. The next day the jaundice had deepened and the urine was diminished and of a deep red colour. The serum was found to be of a reddish hue. At this point quinine was stopped and copious drinks were given with large doses of alkalis. The condition responded well to treatment and the urine cleared gradually and became free from albumen within 4 days. W. Y.

GOLDBLATT (I.). Atebrin in the Treatment of Blackwater Fever.—*South African Med. J.* 1935. June 8. Vol. 9. No. 11. pp. 384–385.

This note describes the treatment given to 13 cases of blackwater fever occurring in Europeans during the period 1934 to March, 1935. Of the 13 cases, 3 were very severe—there was thick, black, tarry urine, marked diminution of urine, persistent vomiting and pronounced general toxæmia—2 cases were mild, and the rest were of moderate severity.

The author states that in all his cases the malarial element was very pronounced, and all previous to the attack of blackwater had been using quinine as an anti-malarial remedy. Goldblatt stopped the quinine at once and attacked the malarial parasite with atebrin. All cases were treated in the following way:—

“The patient was given a large dose of magnesium sulphate. Next a diaphoretic powder consisting of aspirin, pyramidon and pulv. ipecacuanha co. aa. gr. v was administered, and the patient placed between blankets. The patient took a hot drink and heat was applied to the kidney areas. Marked sweating proceeded for about 2 hours, when the patient was thoroughly dried, given a dry sleeping-suit, and left to lie between dry blankets, as diaphoresis generally continued mildly for some time. The application of heat to the renal areas was continued. Atebrin in doses of one tablet (0.1 gram) was given at this stage, and a diuretic mixture made up as follows:—

R.

Pot. citrat	gr.xv.
Spt. aether. nit.	m.xxx.
Tr. digitalis	m.ii.ss.
Decoc. scoparii	ad oz.ss.

Sig. : Half an ounce in water every 4 hours.

"The diet consisted of frequent feeds of citrated milk. The patient was encouraged to drink freely of barley-water, diluted orange drink and other bland fluids. Sodium bicarbonate was added to the feeds and drinks and, when the patient could tolerate it, glucose.

"No special treatment was employed for vomiting, but the patient was encouraged to drink freely despite it. Generally it ceased within thirty-six hours."

Under this treatment a marked improvement occurred and within three days the temperature had become normal and the urine clear in all cases. No relapse was observed. The author remarks that it is impossible to state what effect the atebtrin had upon the course of the blackwater fever as he had no control cases.

W. Y.

MURRAY (A. J.). **Blackwater Fever following Atebrin—a Fatal Case.**
—*West African Med. J.* 1934. Oct. Vol. 8. No. 2. p. 17.

Details are given of a case which supports MOIR's conclusion [*this Bulletin*, Vol. 32, p. 207] that not only are atebtrin and plasmochin incapable of preventing blackwater fever, but they may excite an attack.

The patient in question, a European, aged 34, was admitted to hospital at Kaduna, on the 23rd August, 1934, suffering from malaria. He had suffered from blackwater in the spring of 1933, and acting on medical advice he had taken 5 grains of quinine in liquid form daily ever since. On admission the temperature was 103.6°F., the spleen was considerably enlarged, and vomiting was very troublesome. He was given 10 grains quinine on the morning of the day of admission and again in the evening. He had a restless night, and at 7 a.m. the next day he passed porter-coloured urine. Within a few hours the urine cleared and his temperature become normal and remained so until the evening of the 30th August, when it rose to 99.4°. Thereafter it varied between 97°F. in the morning and 99°F. in the evening. On the 28th August the patient was put on 2½ grains of quinine daily, and this was increased to 5 daily on the 6th September. From the 6th September onwards the swing in the temperature was marked, and on the 10th September the quinine was stopped and atebtrin, 1½ grains three times a day, commenced. The full course was given, but at the end of it the condition was unchanged. On the 15th September, *i.e.*, the sixth day of atebtrin treatment, plasmochin compound was given in addition to the atebtrin. The following day atebtrin was stopped, and 2½ grains of quinine was given with the plasmochin compound. During the night the patient had a rigor and passed blackwater at 6 a.m. the following day. This did not show the slightest sign of clearing up, and the next day the patient died still passing porter-coloured urine.

W. Y.

CORMAN. L'association atébrine-extrait de foie dans le traitement de la fièvre bilieuse hémoglobinurique. [**The Association of Atebrin and Liver Extract in the Treatment of Blackwater.**]—*Bull. Méd. du Katanga*. 1934. Vol. 11. Nos. 3 & 4. pp. 77, 79-82; 113, 115-116.

In these two papers details are given of 4 cases of blackwater fever treated, amongst other things, with atebtrin and hepatrol. All four patients recovered.

W. Y.

DANG-HANH-KIEN. La fièvre bilieuse hémoglobininurique et son traitement préventif par la biocholine intraveineuse. [**Blackwater Fever and its Preventative Treatment by Biocholine Intravenously.**]—*Bull. Acad. Méd.* 1935. Feb. 5. 99th Year. 3rd Ser. Vol. 113. No. 5. pp. 191-195.

The article recommends the intravenous injection of biocholine not only for the treatment of blackwater fever, but for certain cases of malaria as a means of preventing blackwater fever.

Blackwater is very common, especially among the Annamites in the upper regions of Tonking. With the old form of treatment (antivenom serum and calcium chloride) the mortality was 30 to 35 per cent. This figure has decreased greatly since the introduction of the biocholine treatment recommended by Dr. RAYMOND. Details are given of a small number of cases which, in the author's opinion, received benefit from the administration of biocholine. Being convinced that the haemolysis in this disease follows a diminution of red cell resistance resulting from hypocholesteræmia, the author decided to add to his quinine an intravenous injection of biocholine as a preventive in all malaria patients who were generally debilitated, or slightly icteric, or who exhibited hepatic or lumbar pain. Since he commenced this line of treatment he has had hardly any cases of blackwater, although in previous years he had from 15 to 24 cases yearly. The amount of biocholine given at an injection—either subcutaneous or intravenous—was 2 centigrams. W. Y.

VU-DINH-TUAN. Contribution à l'étude du traitement de la fièvre bilieuse hémoglobininurique par les injections intraveineuses d'urotropine. [**The Treatment of Blackwater by Intravenous Injections of Urotropine.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1934. Dec. Vol. 12. No. 10. pp. 940-954.

Since May, 1932, the author has had occasion to treat 18 cases of blackwater fever at Van Yên on the Black River, Tonking. Certain of these cases have been treated in what the author calls the classical method (serum, biocholine, calomel, calcium chloride, etc.) and others by a new method, viz., intravenous injections of urotropine, and still others by a mixture of the two methods.

The urotropine was given intravenously in doses of 1 gm. morning and evening. The drug was first given to a comatose patient on the fourth day of the disease, and as he got better it was subsequently given to seven other cases at the beginning of the disease. The author says the results were "bien curieux." Within half an hour of the injection the temperature fell by half to two degrees; the urine cleared within 22 hours on an average. The earlier the drug is given the sooner is the disease cut short. The jaundice disappears, and vomiting ceases within 12 to 20 hours and convalescence is greatly shortened.

Clinical details of the 18 cases are given. It is noted that of the 10 cases treated in the classical way (biocholine sera, glucose antivenom, etc.) 30 per cent. died; of the 8 cases treated with urotropine none died. [It is instructive to read this paper in conjunction with that of DANG-HANH-KIEN advocating the use of biocholine. The reader can draw what conclusions he pleases.] W. Y.

VAN SLYPE (W.). *Thérapeutique calcique dans la fièvre bilieuse hémoglobinurique.* [**Calcium in the Therapy of Blackwater Fever.**—*Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 85-87.

Details are given of two cases of blackwater treated by the author in December, 1932; these patients were treated in the usual way—serum antivenom, rectal glucose, alkalis by the mouth, abundant fluid to drink, atabrin and plasmochin—and in addition they were given calcium gluconate. The first was apparently a case of moderate severity, but the second was more grave and the urine scanty. Both patients recovered and the author believes that the calcium preparation had something to do with this happy result. W. Y.

FAIRLEY (N. Hamilton) & BROMFIELD (R. J.). **Laboratory Studies in Malaria and Blackwater Fever. Part III. A New Blood Pigment in Blackwater Fever and Other Biochemical Observations.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1934. Nov. 27. Vol. 28. No. 3. pp. 307-334. With 1 coloured plate & 3 graphs. [29 refs.]

These studies were initiated with the object of getting more accurate biochemical and haematological data regarding what is happening at different stages throughout the course of blackwater fever; the present paper gives further information regarding the new blood pigment which the authors have discovered in blackwater cases [this *Bulletin*, Vol. 32, p. 210], and also the result of their investigation of the bilirubin content of the blood and bile, the blood urea, the alkali reserve, and the blood cholesterol in this disease.

One point which might have been brought out more clearly in the previous paper is the naked eye appearance of the plasma and the various factors responsible for the colour changes. Three pigments were concerned, viz., oxyhaemoglobin, methaemoglobin and bilirubin; if present alone the first imparts a red tint to the plasma, the second a brown, and the third a bright yellow. When there is a mixture of these pigments, as in blackwater fever, their resultant colour depends upon their relative and absolute concentrations. This fact is demonstrated in a coloured plate.

The new blood pigment.—This pigment was constantly present, but in variable amounts, over a period of 10 days in the plasma of Case 7. It resembles methaemoglobin spectroscopically, but differs in not being reduced with Stokes' reagent or ammonium sulphide and in never appearing in the urine in demonstrable quantities. It was never found within the corpuscles and differs from sulphaemoglobin in several important respects. KEILIN, who undertook its investigation, reports as follows:—

“ The samples of serum marked 17/XII/33 and 21/XII/33 contain a peculiar haemoglobin derivative with a normal prosthetic group, but the globin portion of the molecule is undoubtedly modified. The spectrum has the general appearance of methaemoglobin with the bands shifted, however, about 60 Ångström units towards the short wave end of the spectrum. Although it does not reduce with Stokes' reagent the compound contains a trivalent iron. It is easily reduced with sodium hyposulphite and gives a typical haemochromogen (globin-protohaemochromogen). Apart from its spectroscopic resemblance to haemoglobin and its trivalent

iron it has no properties of methaemoglobin when tested with alkali, H_2O_2 , H_2S , azide, etc.'"

The history of Case 7, which shows several unique features, is given in great detail and the laboratory findings are recorded in two graphs. Unfortunately, there was no opportunity of examining the plasma during the first 3 days of the disease, but two spectroscopic examinations were made on the 4th day and two on the 5th day, and subsequently the plasma was examined daily until the 17th day and on 6 occasions during the following 15 days. The new pigment was always present until the 14th day, when it disappeared and was not observed again; its concentration, expressed in terms of the dilution factor, varied from 1.5 to 6, as is shown in the graph. As this pigment never appeared in the urine, it was either incapable of being secreted by the kidneys at all or, at any rate, the renal threshold was too high for it to be excreted in a concentration detectable spectroscopically.

Oxyhaemoglobin was present either in small quantities or not at all; the maximum concentration observed was 0.28 per cent. Methaemoglobin was never observed in the plasma, and as the incidence of methaemoglobinuria coincided with an acid reaction of the urine and completely disappeared on the 6th day after the urine became neutral, it is highly probable that it was not "true" methaemoglobinuria at all. The method employed, however, required methaemoglobin to be present in a quantity of 0.665 per cent. before it could be detected, and it is possible therefore that it may have been produced in small quantities and rapidly converted into the new brown pigment.

Other biochemical findings recorded in the graph are commented upon under their appropriate sections later in the paper; but one aspect of special interest was the rapid development in a polyuric type of case of renal acidosis associated with a decreased alkali reserve equalling 33.1 cc. CO_2 per 100 cc. plasma and an inorganic phosphorus value of 7.6 mgm. per 100 cc. on the 4th day of the disease. Nitrogen retention was marked and the blood urea reached the high figure of 340 mgm. per 100 cc. 2 days later.

The Bilirubin content of the blood and bile.—Forty-one estimations of the bilirubin content of the plasma were made in the 7 cases, serial observations being undertaken in 6 of them; the findings are shown in a table. In all the cases the bilirubinaemia persisted for some considerable time after demonstrable haemoglobinuria had ceased—a fact which had previously been commented upon by YORKE, MURGATROYD and OWEN [this *Bulletin*, Vol. 28, p. 1.]

BARRATT and YORKE (1914) [this *Bulletin*, Vol. 5, p. 254], when studying the relation of bile pigment to haemoglobin experimentally in rabbits found that following the intravenous injection of haemoglobin solution there was a distinct and immediate increase, not only in the concentration of bile pigment, but also in the amount excreted. So far as the authors are aware no observations in blackwater fever have been made on the concentration of bile pigment in human bile, either during life with a duodenal tube or at an autopsy. For control purposes estimations on material collected at autopsy were made in which there was no evidence of obstruction to the biliary system. The quantitative indirect reaction showed that bile obtained from the gall bladder in these control cases contained on an average 700 units or 0.35 per cent. of bilirubin. In blackwater Case 3 the bile contained 3,800 units or 1.9 per cent. of bilirubin, and in Case 6, 4,900 units or 2.45 per cent. bilirubin. It is thus seen that the 5- to 7-fold concentration of bilirubin

in the bile of these two cases agrees closely with the experimental findings of BARRATT and YORKE.

Hyperbilirubinaemia was characteristic of all seven cases investigated, the maximal readings in the four non-fatal cases varied from 7 to 26 units, and in the three fatal cases from 20 to 88.5 units (indirect). Two of the three fatal cases showed oliguria, which in one practically amounted to anuria, while the third succumbed to renal acidosis just as water secretion was beginning to fail.

Blood urea.—An increase was observed in all patients, varying from 54 to 79 mgm. per 100 cc. in the three less severe cases, and from 150 to 372 mgm. per 100 cc. in the five severe cases. In the latter group both patients showing polyuria recovered after a prolonged illness, while the others showing a decreased water excretion died. Urea is a powerful diuretic, and the authors believe that its retention and increase in the blood and tissue fluids is probably responsible for the natural tendency to polyuria, which characterizes so many cases of blackwater which recover.

The alkali reserve.—During recent years a few isolated observations have been made to determine the existence or absence of a state of acidosis by estimating the plasma bicarbonate or carbon dioxide combining-power of the plasma in blackwater fever cases. Van Slyke's criteria have been generally followed: he suggested that the normal range varied from 73 to 53 cc. CO_2 per 100 cc., that mild acidosis existed between 53 and 40 cc., moderate acidosis between 40 and 30 cc., and severe acidosis below 30 cc. per 100 cc. of plasma; clinical manifestations were often confined to the last group.

During the present investigation 32 observations on the plasma bicarbonate or CO_2 combining-power of the plasma were made on the 8 cases of blackwater fever. Estimations were always done in duplicate by van Slyke's method, the blood being oxalated and collected under paraffin to prevent chloride shift: a constant decrease in the alkali reserve, varying from 21.8 to 48.0 cc. CO_2 per 100 cc. plasma, was noted in severely ill patients. This lowering of the alkali reserve was associated with urea retention; and in two instances clinical evidence of acidosis developed. Case 9 died of typical uncompensated acidosis with air hunger, and Case 7 developed dyspnoea but recovered with appropriate treatment.

Blood cholesterol.—The average value of 18 estimations of the whole blood cholesterol in 5 very typical cases was 86.5 mgm. per 100 cc., the minimum being 68.0 mgm. and the maximum 109.0 mgm. per 100 cc. There was a persistent hypocholesterolaemia in both fatal and non-fatal cases and the results were not influenced by blood transfusion.

The paper closes with a discussion on the origin and nature of the haemolytic agent in blackwater fever. The authors have shown that methaemoglobin is the predominant pigment present in the plasma in this disease, and that it has an extra-corpuscular origin from oxyhaemoglobin liberated during an intravascular haemolysis of circulating corpuscles. Both the authors, and the reviewer and his colleagues (1930), failed to demonstrate methaemoglobin in the washed corpuscles of blackwater blood containing this pigment, and consequently there is good reason to believe that both methaemoglobin (and the new pigment) have an extra-corpuscular source of origin.

In blackwater there is, therefore, firstly haemolysis of the corpuscle, and secondly conversion of the liberated oxyhaemoglobin into

methaemoglobin, or the allied new pigment. These facts make it highly improbable that we have to deal either with a true haemolysin or a direct drug effect on the corpuscle. A much more attractive hypothesis is that some derangement of metabolism, associated with chronic subtertian malaria, is precipitated by the administration of quinine or plasmoguinine and gives rise to a potent haemolytic substance which first lyses the corpuscles and then acts on the liberated oxyhaemoglobin along the lines already discussed. Whether this action is confined to the backwaters of the circulation or whether it occurs in the general circulation is a matter of conjecture. In the authors' opinion the percentage of total blood pigment is sufficient to explain the blood destruction in terms of a lysis occurring in the peripheral circulation, but the inability to demonstrate either *in vivo* or *in vitro* a lytic substance in the serum or plasma derived from blackwater fever cases may be held to favour the visceral site of haemolysis postulated by the reviewer and his colleagues. It must, however, be remembered that the negative results may depend upon the immediate fixation of the haemolytic agent by the corpuscles or on its fluctuating concentration, which would add to the difficulty of its demonstration unless the specimen happened to be collected at exactly the right time.

YORKE, MURGATROYD and OWEN (1930) have shown that several haemolytic crises rather than one isolated haemolysis characterizes blood destruction in blackwater fever, and the authors have confirmed this in several of their cases; but not all cases fall into this category, as in two instances the haemolysis remained unabated until death. Evidently the haemolytic agent may be present in variable quantity in different cases and at different stages of the same case. Apparently, following a haemolysis the haemolytic agent is decreased or entirely used up, and time is necessary for its production and accumulation in a concentration adequate to produce another haemolytic crisis.

Writing on the subject of the disposal of blood pigment, the authors say that it is generally agreed that in any intravascular haemolysis only a very small proportion of the liberated oxyhaemoglobin appears in the urine. Much of the blood pigment is, of course, dealt with by the reticulo-endothelial system; here the haemoglobin is considered to be converted into an iron-containing moiety, haemosiderin, which is ultimately deposited in the cells of the liver, spleen and kidney, and an iron-free pigment, haemobilirubin, which circulates in the blood and is converted by the polygonal cells of the liver into cholebilirubin with resulting polycholia. In the present series of cases abundant evidence of hyperactivity of this mechanism was found.

[It is impossible in a summary of moderate length to do justice to this valuable paper. It is greatly to be hoped that all who have to deal with cases of blackwater fever will study it carefully in the original. This might have two results—both excellent in the reviewer's opinion: Firstly, it might encourage a few serious students of the disease to attempt to make similar observations for themselves and thus, by collecting reliable data, make a definite contribution to the solution of the mechanism of this most baffling disease; and, secondly, it might discourage the many who plunge into print for no discoverable reason, except to demonstrate their complete ignorance of the disease and to add to the enormous mass of rubbish which is the chief characteristic of the literature relating to blackwater fever.]

DEUTSCH (Béla). Ueber Häoglobinkonzentrationsbestimmung im Blute. [The Estimation of the Haemoglobin Concentrations of Blood.]—*Biochem. Ztschr.* 1934. Nov. 14. Vol. 274. No. 3/4. pp. 299–304. With 1 fig.

DÉNES (1932) converted the haemoglobin of blood into haemochromogen and estimated the light absorption of the haemochromogen solution. In order to satisfy himself that this procedure is actually suitable for the determination of the haemoglobin concentration of blood, Deutsch has compared the haemoglobin concentration values given by Dénes' method with those given by methods based upon the oxygen capacity of the haemoglobin. The conclusion reached is that the method is satisfactory. [The paper, which is rather technical, should be consulted in the original by those interested.] W. Y.

BLACKIE (W. K.). The Reticulocytes in Blackwater Fever.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. April 17. Vol. 28. No. 6. pp. 571–578. With 1 graph.

Haematological studies made on 4 cases of blackwater fever showed that a vigorous reticulocytosis followed in the wake of the haemolytic phase of the disease.

A brief clinical outline is given of each of the 4 cases, and the observations made on each are given in tabular form. The observations consisted of (1) red cell count, (2) haemoglobin estimations, (3) colour index, (4) size of red cells, and (5) determination of percentages of reticulocytes. In each case a long series of observations was made. The findings suggest that during the stage of active haemolysis the disease exerts an inhibitory influence on erythropoiesis as manifested by the low reticulocyte counts recorded during this period. Moreover, this inhibitory effect is maintained in spite of the severe degree of anoxaemia induced by gross lack of red cells, and in spite of the stimulant action of free haemoglobin or its derivatives. With the cessation of the haemolytic process active erythropoiesis is established and the reticulocyte count rises with extraordinary rapidity. The maximum response in the 4 cases varied from the 6th to the 14th day after the commencement of erythropoietic activity. In the 3 severe cases the maximum figures were, respectively, 50·8, 52·2 and 53·6 per cent., whilst in the less severe cases it was 26·2 per cent. Thus the magnitude of the reticulocyte response is determined to some extent by the degree of anaemia; another factor of importance is, however, the hypertrophic state of the bone marrow. W. Y.

KRISHNAN (K. V.) ; GHOSH (B. M.). The Reticulo-Endothelial System in Malarial Haemoglobinuria of Monkeys [KRISHNAN].—*Indian Med. Gaz.* 1935. Apr. Vol. 70. No. 4. pp. 193–197. [13 refs.] Part II. The Relation of Spleen to Haemoglobinuria [KRISHNAN & GHOSH].—*Ibid.* pp. 197–200.

i. In the course of previous investigations the impression was gained that the incidence of haemoglobinuria in monkeys infected with *Plasmodium knowlesi* was higher in those animals in which experimental damage or dysfunction of the reticulo-endothelial system was caused. This impression led the authors to investigate the matter further. *P. knowlesi* causes a low grade infection in *Silenus irus* and *S. radiatus*, but an intense and rapidly fatal infection in *S. rhesus*. In the latter species a certain number of animals (60 per cent.) dying of

severe infection developed haemoglobinuria. The authors ask how it is that all rhesus monkeys, which develop a heavy infection, do not exhibit haemoglobinuria? Is it because of their increased capacity to deal with haemoglobin, and, if so, what is the basis of this increased capacity?

The observations recorded in this paper were made on a series of 25 *S. rhesus* infected with *P. knowlesi*. The technique used for identifying reticulo-endothelial cells was the supravital staining technique of Napier, Krishnan and Lal (1932). The cells were classified as monocytes and histiocytes according to their capacity to phagocytose neutral red. Total and differential counts were also made. Serial observations were made from the day the animals first showed parasites in their peripheral blood to the day of their death or recovery.

The 25 monkeys are divided into two groups, viz., Group I, consisting of 14 animals which developed a heavy infection and haemoglobinuria; and Group II, consisting of 11 monkeys not developing haemoglobinuria despite a heavy infection. By the term "heavy infection" is meant a parasite count of 0.2 to 0.5 million per cmm., corresponding to over 50 parasites per microscope field. As monkeys of both groups tended to die if left untreated, quinine was administered by injection to approximately half the number in each group. The results of the observations are summarized in two tables. Table I shows that there is a distinct difference in the counts of the reticulo-endothelial cells in the two groups of monkeys studied. In the pre-haemoglobinuric state of the monkeys in Group I there is a reduction in the number of reticulo-endothelial cells compared to Group II monkeys. In the latter group the mobilization of the reticulo-endothelial cells was marked and haemoglobinuria did not result, although the monkeys showed as heavy an infection as did the monkeys of Group I. Furthermore, it was noticed that the reticulo-endothelial cells in Group I monkeys, just before haemoglobinuria occurred, were functionally less active, the amount of neutral red ingested by them being very much less than that ingested by the reticulo-endothelial cells of Group II monkeys.

The author concludes from this observation that in the pre-haemoglobinuric state there is a depression of function of these cells. Again, it is interesting to note that in Group I monkeys, which developed haemoglobinuria, the maximum intensity of infection was reached in a very much shorter time than in Group II monkeys, which did not develop haemoglobinuria, *i.e.*, 4 days in Group I as compared with 7.5 days in Group II. The general conclusion drawn from these observations is that a damaged reticulo-endothelial system is a prerequisite to malarial haemoglobinuria.

Table 2 shows the fates of the infected monkeys of Groups I and II, which are divided into Subgroups A and B, according to whether they were treated or untreated. The mortality was higher in Group I than in Group II and treatment produced better results in the latter group. The cause of these differences was investigated by a study of the reticulo-endothelial cell response after haemoglobinuria and treatment.

ii. In this work the effect of the removal of the spleen in monkeys infected with *P. knowlesi* was studied. In all, 118 monkeys were used, and of these 56 were splenectomized and 62 served as controls. Approximately, half the number of animals in the splenectomized and non-splenectomized groups were treated with quinine when the infection reached a definite intensity.

The results are summarized in a table, from which it appears that the incidence of haemoglobinuria is significantly higher in the splenectomized than in the non-splenectomized groups. It is also interesting to note that haemoglobinuria occurred in the splenectomized *irus* and *radiatus* monkeys, which normally never exhibit this sign. Treatment with quinine reduced the incidence of haemoglobinuria in all cases, but did not prevent it.

The paper closes with a general discussion of these results and of their bearing on blackwater fever in man.

W. Y.

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- BRENNAN (C. H.). A Note on a Case of Haemoglobinuria in a Ukamba Native. —*East African Med. Jl.* 1934. Oct. Vol. 11. No. 7. p. 226.
- GIUNTA (Giuseppe). La febbre biliosa emoglobinurica in Somalia ed i suoi rapporti con la malaria.—*Arch. Ital. Sci. Med. Colon.* 1934. Dec. 1. Vol. 15. No. 12. pp. 899-914. [10 refs.] English summary (4 lines).
- HANIFAH (Abu). Een geval van zwartwaterkoorts in Midden-Sumatra.—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. July 8. Vol. 75. No. 14. pp. 1164-1172. [17 refs.]
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REVIEWS AND NOTICES.

DEIMER (Johann Heinrich). **Over blotypen van *Anopheles maculipennis* Meigen, in het bijzonder in westelijk Nederland een taxonomisch onderzoek.** [Biotypes of *A. maculipennis* in the Western Netherlands.] [Thesis for Doctorate of Natural Science at Leiden University.]—256 pp. With 1 plate, 11 figs. & 25 graphs. [11 pages of refs.] Amsterdam : N.V. Boekhandel W. Ten Have.

The argument, which is here presented in full, may be summed up as "The Race Problem, Applied to *Anopheles maculipennis*." That problem, fortunately, does not arise in the case of all anopheles, but relates especially to those of extensive and widely differing distribution. Its great importance lies in this, that difference of race and racial habit is invoked to explain the possibility of "Anophelism without Malaria." As is natural, in a doctorate thesis of the University of Leyden, the subject matter deals mainly with the problem in its application to the Netherlands. Malaria is not endemic throughout the Netherlands—any more than it is throughout the greater part of Europe—and may be said to be confined to North Holland, Western Friesland and the country East of Gronigen. The mosquito concerned with its transmission in the Netherlands is the well known *Anopheles maculipennis*. Two races of this mosquito come into question, *atroparvus*, the small winged and *messeae*, the large winged mosquito. Many characters have been investigated which should provide the means and foundation for immediate differentiation of these races. It must be stated here that the author, in the first part of his work, uses the term "race," or as the case may be "variety," provisionally and that definition of "species," "race" and "variety" receives special consideration later in a special chapter.

The differences between the two races are worked through on a morphological and a biological basis. The latter consideration has given rise to the conception of the "zoophile," or misanthrope, and the "androphile" mosquito. These conceptions lead naturally to the institution of antimalaria measures by "zoophylaxis" through the provision of a sufficiency of the alternative mosquito host, the cow, and "stable diversion" *plus*, of course, treatment of breeding places. Two biological races of *A. maculipennis* may exist, the one positively and the other indifferently zoophile. If that be so, it is the indifferently zoophile mosquito which is dangerous to man. Positively zoophile races are said to have a maxillary index (mean number of teeth on the maxillae) of under 14 and the indifferent race of over 14. The distinction is questionable. It has long been known that malaria is more apparent in districts where the polder water is brackish only and not in those where it is definitely salt. This fact has been expressed more or less quantitatively in the statement that a 0-40 per cent. admixture tends to the production of a zoophile type. In Leyden (no malaria) the water is salt, in Bolsward (high malaria) is brackish.

Other considerations of a bionomic type such as the effect of temperature and humidity on the life of the mosquito are considered critically. "Gonotrophic" characters are also taken into account. Thus, in the Netherlands, *atroparvus* shows "gonotrophic dissociation" that is to say, continuance of blood feeding even with the suspension of ovulation which sets in with hibernation, while *messeae* on the contrary exhibits "gonotrophic concordance," by which is meant simultaneous cessation

of ovulation and blood feeding during the winter months. Experimental work on the subject during these months, but with temperature raised to 26–27°C., showed that the mosquitoes fed richly on blood, but whereas *atroparvus* laid many eggs *messeae* and *typicus* were definitely slow in ovulation. Experiments on interbreeding of races receive special treatment in a special chapter and it has been suggested that in the neighbourhood of Leyden, where a mixed population of mosquitoes exists, the finding of a number of moderately large *atroparvus* mosquitoes might mean crossing between *messeae* and *atroparvus*. It is interesting to have the various described races of *A. maculipennis* separated out as regards their relation to malaria and their biological characters:—Thus *messeae*, *melanoon*, *typicus* and *atroparvus* are animal maculipennes. Where they occur, and where there are at the same time sufficient cows and suitable stables, the contact of the mosquito with man is practically broken and “anophelism without malaria” is the result. In the case of *messeae* there is also a “gonotrophic concordance” which prevents the autumnal infection. *Labranchiae* and *elutus*, on the contrary, are human maculipennes and are the promoters of severe endemic malaria.

The bionomic characters of mosquitoes are perhaps the most interesting but the morphological characters also receive in this work very considerable attention. An extensive treatment of these for eggs, larvae, pupae and imagines, by statistical methods, with frequency distributions, their constants and associated errors, is incorporated and is very important in a taxonomic sense.

Chapter II begins with a statement of questions that have to be answered and these show the general trend of the subject matter in subsequent chapters:—

(1) Is the small-wing *Maculipennis (atroparvus)* of the malaria districts of the Netherlands identical with that of the malaria-free districts and could crossing between *messeae* and *atroparvus* explain the absence of malaria? (2) What are the characters of the offspring obtained by crossing *atroparvus* with *messeae*? (3) Ought *atroparvus* and the other types of *Maculipennis* to be regarded as races, varieties or species and (4) Is *A. maculipennis*, as a morphologically delimited Linnean species, a subjective philosophic abstraction or an objective reality?

An answer to the last of these questions is to some extent given by the nomenclature proposed by the author for the “races” of *A. maculipennis*. He departs from the Linnean binary system to adopt a ternary nomenclature and subdivides them as:—*A. maculipennis typicus*, Martini, Missiroli and Hackett 1931; *A. maculipennis messeae*, Falleroni 1926; *A. maculipennis melanoon*, Hackett 1934; *A. maculipennis labranchiae*, Falleroni 1926; *A. maculipennis atroparvus*, van Thiel 1927; *A. maculipennis elutus*, Edwards 1921.

The main points brought out in the author's summary of his own position are:—

1. Whereas *messeae*, *melanoon* and *typicus* are the so-called “animal maculipennes,” *atroparvus*, although primarily a stable mosquito, can in some districts maintain an endemic malaria. *Labranchiae* for Italy and *elutus* for S.E. Europe are “human maculipennes” and responsible for endemic malaria.

2. The fat body in *messeae* is fully mature by September but in *atroparvus* is still small at the end of October. Investigation of the state of the fat body in *atroparvus*, from a malarial district as compared with that in a non-malarial district gave no confirmation of the idea that crossing took place between *messeae* and *atroparvus*. Neither did the experimental

crossing of *atoparvus* with *messeae*: the character of the progeny (claspette spine; pupal skin spine) showed dominance of *atoparvus*.

3. *Atoparvus* and *messeae* are morphologically very similar. Although constant structural differences appear to exist between them, in eggs, larvae, pupae and imagines, still the "means" of the different characters of the two types came very close to one another, when the conditions of growth (natural or artificial) were the same.

4. Malariologists call the constant types of *A. maculipennis* "races" and accord to each of them the systematic rank of "variety." . . . The definition of a species receives no uniform acceptance. From a strictly morphological point of view *A. maculipennis* is a species and its types varieties, but from the purely physiological standpoint three kinds can be delimited (a) *atoparvus*, *labranchiae* and *elutus*, (b) *messeae* and *melanoon*, and (c) *typicus*. A compromise is suggested in the nomenclature of the types. It is a compromise between the morphological and physiological standpoints and employs a ternary mode of naming.

5. The complex type of *A. maculipennis* is neither an objective reality nor a subjective abstraction but it possesses a real total characterization as also do the biotypes.

W. F. Harvey.

BARBOSA (Amando) & ARJONA (Benito López). **El paludismo en el primer año de la vida.** [Malaria in the First Year of Life.]—138 pp. With 1 fig. & 8 graphs. [Bibliography.] 1935. Plasencia, Cáceres: Imprenta "La Victoria" Valdegamas número 20. [Ps. 6.]

This is a most interesting study, well documented, carried out by men who have made the most of good opportunities for observation. These observations are expressed clearly and the reasons for the deductions which the authors make are given, the diction is plain and, in short, this small book is eminently readable and instructive and, in the reviewer's opinion, might with advantage be translated into other languages so that the knowledge and advice contained might reach a wider circle.

Malaria in the very young presents certain special characters of which many tropical practitioners, who have learned of the disease among adults and at home, are quite unaware; this applies not only to diagnosis but also to the adverse effects on nutrition and development and on other diseases.

This book is divided into ten chapters, each of which contains plenty of food for thought. The first discusses the question of malaria as a cause of abortion and premature labour, for it may cause death of the foetus or expulsion of an infant feeble in constitution, and liable to succumb to what would be a mild infection to a healthy child. A few figures are given: Of 152 pregnant women systematically treated with quinine *per os* and 62 by subcutaneous and muscular injection none aborted; of 57 with severe malaria, untreated, 12.5 per cent. [? 7] aborted and 35.5 [? 20] gave birth prematurely; 40 of the children were born dead; of 68 with untreated benign malaria [? mild attack or *P. vivax* infection] 9.7 per cent. aborted, 33 per cent. had premature labour and half the children were born dead; of chronic relapsing cases treated [number not stated] 1.8 per cent. aborted, 21 births were premature and one-third of the children were born dead; of similar cases untreated the corresponding figures were 16, 40–47 and 50 or more per cent. There are various hypotheses as to the reason for malaria interrupting gestation; fever leading to uterine contraction,

anaemia of the mother leading to death of the foetus, toxins initiating contractions, etc.

Chapter II deals with Congenital Malaria. Many authorities are quoted and their views given and there is an admirable short summary in the course of which the authors state: "Congenital malaria undoubtedly exists but the percentage of cases is very small." All three forms of the plasmodium have been seen in the new-born, a large accumulation of them in the placenta appears to favour the condition but is not a *conditio sine qua non*. Next follows a chapter on Immunity. The authors conclude that there is no cross-immunity between the three species, that persons premunized against the strains present in one region have no effective immunity against the strains of another, and that if real immunity exists it must be very exceptional. Further, that any immunity which may have been acquired rapidly disappears when the parasites have been got rid of, that the degree of immunity is greater after spontaneous cure than after cure by drugs; finally, that immunity is acquired more quickly to *P. vivax* than to *P. malariae* and to the latter more than to *P. falciparum*.

As regards Morbidity and Mortality in the young, sex is shown to have no influence; vital statistics are given with respect to sex, age in months, time of year, etc., in Spain as a whole and in Cáceres in particular. In the first and second three months children have about the same morbidity rates, thereafter they increase in successive trimesters. Chapter V on the Clinical Aspects of Malaria in children is highly interesting. Convulsions or vomiting often replace the initial rigor, or there may be marked cyanosis lasting for 10-15 minutes. Some authorities say that the febrile period is short, but in the experience of the authors it was as long as in adults, and at times longer. The benign tertian infection can produce "pernicious attacks" in a child, the temperature curve is often irregular. In 65 per cent., however, it was typically tertian, in 32 per cent. it was quotidian, in 3 per cent. it was continued; occasionally it was irregular; the quartan type was rarely seen in children under 12 months. Splenomegaly was present in about 80 per cent. of cases, it was more marked in *vivax* than *falciparum* infections, but the degree increased with the number of attacks; occasionally it was almost the first sign. Leucopenia was found in about one-third of the cases of uncomplicated malaria in children. Dyspepsia, vomiting and diarrhoea, perhaps choleriform, are common symptoms, and in children with gastro-intestinal disturbance the malaria is more severe; loss of weight may be marked. Labial herpes is not uncommon; urticarial, scarlatiniform and morbilliform rashes are spoken of, but these, the authors believe, are drug rashes (quinine, atabrin, plasmoquine) rather than due to malaria.

Progress depends on (1) the promptness with which the diagnosis is made and treatment undertaken, (2) the nature of infection, (3) whether the attack is primary or a relapse, (4) intercurrent conditions, (5) the type of feeding, whether natural or artificial. As regards the second of these the authors maintain that in Cáceres there is not much difference in virulence between the strains of *P. vivax* and *P. falciparum*. Treatment is detailed in Chapter IX, both of the primary attack and of the relapse. From this, as summing up the authors' opinions, the following extract is translated:—

"Of the several modes of administering quinine in the treatment of malaria: The *tracheal* route is merely a therapeutic curiosity; the *rectal*

is of value only in grave cases in which nausea prevents oral administration; of the *intra-dermal* we have practically no knowledge; the *sub-cutaneous* has little to recommend it, for it has no advantages therapeutically and is liable to cause abscess and sloughing; *intra-spinal* merely to complicate a treatment which is fairly simple; the *intravenous* route, as MARCHIAFAVA & BIGNAMI maintain should be reserved for exceptional cases of pernicious malaria in which, owing to a state of collapse, there is hope of rapid absorption by the tissues and of immediate action on the parasites in the blood stream in the viscera and in particular the nervous system. In very young children, however, this is far from easy and we are driven to conclude that in them the only possible routes are the oral and the intramuscular."

"Contrary to widespread belief *administration per os will always be the method of choice in the treatment of malaria in infants*. We do not understand the affirmation of FISCHER and others that the best way of treating malaria in infants is by injection, since the many advantages claimed for intramuscular injection—certainty of dosage, greater efficacy, surety of absorption—have yet to be demonstrated." Later they state, "We declare emphatically that quinine and other specific remedies should be given parenterally only when the buccal route is impracticable."

For first attacks of benign tertian they give 20 cgm. of quinine [the salt used is not specified] daily to children under 4 months, 30 cgm. above that age, for eight days to well nourished and for ten days to wasted children. Treatment by atebirin should not exceed 8 days; 5 cgm. daily to those under 6 months, 10 cgm. for those older, given in two doses after food. After the course no antimalaria remedy should be given till a recrudescence occurs, then as before but using whichever (quinine or atebirin) was not used in the first attack. In relapses the rules of the Malaria Commission of the League of Nations, which are quoted, are to be followed as closely as the state of the patient will allow.

In subtertian infections: for the primary attack quinine alone for 7 days, quinine and plasmoquine for another 7, and then quinine alone again for a further like period, the dose being 20–30 cgm. daily of quinine and 0.5 cgm. plasmoquine under 6 months, 1 cgm. to those above 6 months. If there is doubt as to whether the infection is one of benign or malignant tertian the patient should be treated for the latter. Atebrin should not be given to children with digestive and intestinal disturbance and, when atebirin has been used, plasmoquine should not be given till a fortnight has elapsed and then in a small dose 0.0025–0.005 gm. daily for 5 days.

In conclusion, they affirm that quinine can be given to pregnant women in the usual doses without fear; that abortion following administration of quinine is ascribable not to the drug but to the fever, and that quinine is the best prophylactic to ensure a normal pregnancy in women suffering from malaria.

Illustrative cases are not numerous but those given have been carefully chosen; there is a good and full bibliography. H. H. S.

PESSÔA (Samuel B.) & MEIRA (João Alves). **A eosinophilia sanguinea.** 165 pp. [Bibliography.] 1935. S. Paulo, Brasil: Sociedade Editora Medica Ltda. Caixa 1.574.

This is a very full monograph on eosinophilia and leaves one wondering whether the subject is of sufficient importance to warrant such a detailed and exhaustive treatment. The work is divided into four

parts, the first being of a general and introductory character on eosinophilia in man. This contains as much as most persons know ; it starts with defining the normal count and the conception of eosinophilia in man and then treats of the conditions under which the excess is found, including various infections, allergic states, organotherapy, X-ray treatment, rickets, gastric and duodenal ulcer, chronic arthritis, endocrine affections and so on. Indeed, it would be almost a shorter list to give the conditions in which this sign is not found. Where it occurs in so many its value in diagnosis diminishes inversely. [The reviewer remembers a teacher of medicine whose favourite question was " What are the causes of enlargement of the spleen ? " and the number increased session by session till the number reached between 50 and 60, by which time of course its value in diagnosis was reduced to vanishing point.]

Part II discusses eosinophilia in parasitism, especially helminthiasis, and Part II experimental eosinophilia. This is valuable because the normal leucocyte counts of 17 species of animals are given, among them those of the horse, cattle, goat, pig, rabbit, guineapig, Brazilian opossum, coati, capibara, cat, dog, rat, macaque, and camondongo, with the number of animals on which the findings are based and the author who carried out the estimations.

Part IV deals with experimental data obtained in rats. It gives the normal leucocyte formula in these animals, the eosinophile increase in those with helminthic infestations, the counts before and after injection of substances believed to produce eosinophilia, *e.g.*, ascaris extract, and lastly the effect of splenectomy. There is an ample bibliography of 206 references.

H. H. S.

TROPICAL DISEASES BULLETIN.

Vol. 32.]

1935.

[No. 12.]

PLAGUE.

RUSSELL (A. J. H.). **Plague in India.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 725–733.

WU LIEN-TEH. **Pestilence and Plague in China.**—*Ibid.* pp. 735–759. With 1 map.

WU (C. Y.). **The Occurrence, Distribution and Seasonal Prevalence of Rat-Fleas in China (with a Note on their Relation to Bubonic Plague).**—*Ibid.* pp. 761–771. With 4 charts. [15 refs.]

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. **TRANSACTIONS NINTH CONGRESS, NANKING, CHINA, 1934.** Vol. 2. pp. 773–784.—**Round Table Discussion on Plague** [PANDIT (C. G.), Chairman].

RUSSELL (A. J. H.).—This presentation of the whole subject of plague is full of important pronouncements and would almost demand that each of its successive paragraphs be summarized.

Plague has been responsible for over 12 million deaths in British India during the last 38 years but both incidence and mortality have a rapid and progressive downward trend. Percentages of the total mortality from 1898 to 1933 are 50, 35, 13, and 2 for the periods 1898–1908, 1909–1918, 1919–28 and 1929–1933. Over these 38 years there appears to have been also a rapid and progressive immunization of the rat population and in view of this occurrence "it is difficult to estimate the part played by the usual sanitary measures in reduction of the disease." The comparative immunity of certain of the Indian provinces or even, as in the case of Assam, its entire immunity in spite of the presence of a susceptible rat population would seem to point to other circumstances. These may perhaps be found in other biological factors, "influences acting to the detriment of the flea carrier." Bengal is a province which has gradually lost its infection. [It would be interesting to know whether there exists in that province, as may be the case throughout the ports of the world, a subliminal infection in the rat population insufficient to reproduce either epizootic or epidemic.] "The comparative freedom of the whole eastern seaboard of India, of northern Burma, Assam, Bengal, the S.E. parts of Bihar and Orissa and the Western areas of the Punjab and Upper Sind" is a remarkable epidemiological phenomenon. Climatic factors are undoubtedly potent in their effect on the seasonal subsidence of

plague and may probably be summarized in the statement that "saturation deficiency is a measure of the drying capacity of the air, a high degree of which is inimical to the life of fleas. The decline of plague everywhere in India during the hot season is therefore due to high temperatures and saturation deficiencies." Forecasts of probable plague incidence are now successfully made on this basis.

The statistical figures of the value of anti-plague vaccine in India have now reached commanding proportions and Russell considers that the published tables of results provide "comparable and reliable figures for inoculated and uninoculated groups of populations": he quotes TAYLOR's estimate that plague prophylactic vaccine "gives roughly a four-fold protection against attack and an eight-fold protection against death." [The populations compared, however, are not of the strictly "alternate case" type and may have presented some selection: the experience in the Netherlands Indies does not seem to have been so favourable.]

Research work on plague in British India is very vigorously pursued. Confirmation of the statement that greater value is to be attributed to *Past. pestis* grown at 37°C. than at 27°C. has not been forthcoming. Anti-bacterial sera are having increased attention, and among these especially plague serum. The method of standardization of such serum aims at "the measurement of the minimum amount of a given serum that would protect more than half of the animals inoculated against a measured amount of test dose of plague given at the same time as the serum but separately from it." A plague serum has been tried out with, so far, promising results: "100 cases treated with 32 deaths (32 per cent.) and 77 controls with 53 deaths (69 per cent.). . . . As far as possible every alternate admission to the infectious diseases hospital was given serum."

The perpetuation of epizootics or enzootics is a very important plague study. "Definite evidence of smouldering epizootics all the year round has been found in some of the larger villages." These are probably due to the "persistence of infection in rat-fleas which have been proved capable of carrying over plague infection for more than four weeks even under conditions of starvation." There does not, however, seem to be much evidence that wild rodents such as gerbils, moles, field mice and squirrels have played much part as off-season reservoirs. A reference to the comparatively recent studies on retention of infection in, and the climatic conditions of rat burrows is made. The successful fumigation of rat burrows with cyanogas [this *Bulletin*, Vol. 31, p. 878 and *ante*, p. 453] concludes this informative survey.

WU LIEN-TEH.—In the introduction to this address we find the statement that "plague in China being restricted at present to a few areas and showing little tendency to spread beyond these foci, its public health importance seems limited as compared with that of certain other diseases." The history of plague "seems to show that most, if not all, plague outbreaks in China can be traced back to Central Asia." Further we learn that plague "once it had become fairly entrenched in the coastal regions remained restricted to the ports . . . and did not travel any great distance inland." The author points out that this is not surprising when we consider how easily rats can be transported by ships as compared with the possibilities of slow moving inland traffic. The importance of this is referred

to later in connexion with the possible dangers of the rapid development of railway and other fast-moving vehicular traffic. It is interesting to find that the Director of the National Quarantine Service of China is emphatic in saying that plague outbreaks "were invariably preceded by and in causal connection with, epizootics among the domestic rodents" and that "excluding again the areas with tarabagan plague, *X. cheopis* may be considered as the principal, in most as the sole, vector of infection." A further support to this, the general contention, is given in the final round table conference by POLLITZER who says: "I am very sceptical as to the claim that plague in North Africa spreads without the intervention of rats. . . . The absence of rat plague is apt to be more apparent than real."

WU (C. Y.).—Although three species of fleas, *X. cheopis*, *Leptopsylla musculi* and *Ceratophyllus anisus* are found to occur in large numbers in China the main rôle in the production of human plague is accorded to *X. cheopis*. Climatic factors and seasonal incidence are both considered in their bearing on rodent fleas and some illuminating graphs are given of the simultaneous percentage seasonal distribution of rat fleas (*cheopis* and *anisus*), rat plague and human plague. The plague season in southern China coincides with the prevalence of *X. cheopis*, but in Shanghai this flea is rarely found during this season. It is otherwise, however, for China to the north where there is "a dangerous coincidence with the period comparatively suitable for the spread of plague in Shanghai." Experience has shown, nevertheless, that "the epidemics in the north spend their energy at the spot rather than tend to invade the maritime regions. As long as this state of affairs prevails, a recurrence of epidemic plague in Shanghai is unlikely."

ROUND TABLE DISCUSSION.—Most of the agenda set out for discussion were discussed shortly by those present and interesting replies were given as to researches and opinions held in the several countries.

W. F. Harvey.

TAMPI (N. Krishnan). **A Report on Plague in Peermade (Travancore State).**—*Indian Med. Gaz.* 1935. July. Vol. 70. No. 7. pp. 383-389. With 2 maps.

This report describes what appears to have been the first (1932) serious outbreak of plague in Travancore State. The district affected, Peermade, forms part of the highland division of the State and the conditions prevailing may be said to be favourable to the outbreak of plague. "Opportunities are numerous for close association between rats and man. The houses are crowded together, dark and ill-ventilated. The holes in the floor and the ceiling offer excellent shelter for rats. The coolie lines are insanitary and overcrowded and the tea bushes around the lines also offer good shelter for the rats. Every estate has one or more rice stores all teeming with rats." The prevalence of *X. cheopis* is as high as 72 per cent. on *Rattus rattus* caught in the area, a figure which "is far higher than is necessary for effective plague transmission as observed in other localities in India." The author thinks that there is serious danger of the Peermade hills becoming a permanent centre of plague infection.

W. F. H.

KARVE (J. V.) & SUNDARARAJAN (E. R.). **Endemicity of Plague in Mysore State. Part I.**—*Indian Jl. Med. Res.* 1935. July. Vol. 23. No. 1. pp. 21–55. With 2 graphs & 2 coloured maps. [17 refs.]

This is a valuable study of plague as it has affected an important Indian State. The authors have made an extensive statistical survey and have investigated especially the questions of endemicity and the possibility that the State is the source of plague for surrounding districts. Their communication is a preliminary one and is still incomplete. W. F. H.

IYENGAR (M. O. T.). **The Identification of the Common Rat-Fleas of India.**—*Indian Jl. Med. Res.* 1935. Apr. Vol. 22. No. 4. pp. 675–686. With 5 plates & 11 figs.

This is a simple illustrated key intended merely to facilitate quick identification of the common genera of Indian rat fleas and the species of the more important genera. The necessary technique is described; simple characters only are used for differentiation; and the paper is illustrated by excellent photographs and drawings.

V. B. Wigglesworth.

TSURUMI (M.). L'épidémie de peste au Manchoukouo en 1933. [**Plague in Manchukuo in 1933.**]—*Bull. Office Internat. d'Hyg. Publique.* 1935. Feb. Vol. 27. No. 2. pp. 254–256.

The epidemic of plague which prevailed in Manchukuo from August 1933 to January 1934 approached in its severity that of 1920–21 and claimed approximately 1,800 victims with a calculated mortality of 1,546. Up to the present the region east of the interior of Mongolia has been regarded as the only focus of the disease, but the province of Nungan is now regarded as another. The ground squirrel has, since 1928, been regarded as the intermediate animal of transmission, but this report seems to consider the possibility of rats also being concerned in the transmission of plague to man. At least half of the cases seem to have been bubonic but there were certainly numerous cases of septicaemia without enlargement of lymph nodes. Certain cases of pneumonic plague were reported from Nungan and Tungliao. Pneumonic plague apparently may be so rapidly fatal that the septicaemic state, which usually accompanies it, has not time to develop and the heart blood proves sterile on culture. The incubation period of eight cases of bubonic plague varied from 3 to 7 days. W. F. H.

BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1935. Feb. Vol. 27. No. 2. pp. 257–267. With 1 map.—Enquête sur la peste en Afrique et sur le rôle des rongeurs sauvages et domestiques dans sa propagation. La peste en Angola [JORGE (Ricardo)]. La peste dans le Kenya et l'Ouganda pendant les années 1929–1933 [KAUNTZE (W. H.)]. [**Plague in Angola, Kenya and Uganda.**]

A continuation of the report on the questionnaire on Plague in Africa [see this *Bulletin*, Vol. 31, p. 875].

ANGOLA.—Plague attacked Angola rather late at the beginning of 1921, making its entry by the principal port and capital of the colony, St. Paul de Loanda. The epidemics which occurred in this town and in other ports were of the usual type, that is, they followed a rat epizootic. Selvatic plague, the plague of the wild rodent, has been recorded. Especially notable was a wave of migration of gerbilles from the South African veld, proceeding at the rate of 200 miles a month and sowing plague as it went, but productive of only two cases of human plague in Angola territory. The article concludes with the proclamation on plague, issued to the natives of Angola and couched in language suitable to the mentality of those addressed :—

"Listen people of Cuanhama, Cuamoto, Humbe, Xinga, to these words of the doctors of the Portuguese Government. You have heard of a very serious sickness which has raged for the last nine months in Ondonga, Ombarrantu and Ongandjera. This sickness is among the rats which are dying everywhere, in plantations, gardens, plots and houses. The sickness passes from rat to rat and from rat to man by fleas. The Portuguese Government, with the welfare of its people at heart, has not waited for the sickness to cross the frontier and kill their people. As soon as it had heard that the sickness was at hand on the frontier it sent doctors with vaccines, medicines, carriages and much money—more money than could be collected by 20 years of tax in all Bas-Cunene—so as to be ready for the sickness and prevent the terrible results which it brings. Fear the rats: the gerbilles (mah'êto), the multimammate mice (muco), the situta, the catata, etc. If you do not want to be ill keep your houses always clean, do not let rats get near food, clear away the galleries of the rat burrows in the huts and round about to a distance of 500 metres. Leave your huts as soon as you find in them a dead rat. Tell the doctor and the post-master: the post-master will let the doctors know and they will come immediately in their cars. Those houses in which plague occurs ought to be left with only one native, who should be vaccinated, to look after the sick person. Make your way to the doctor or the post-master. Oh! people, the doctors only want to keep you well! Pursue the rats. Protect their natural enemies: the mongoose, the wild cat, the owl, the rat snake and especially the fox. Get yourselves vaccinated. Take the advice of the doctors. Be grateful to the Portuguese Government for the care which they are taking to preserve your lives!"

KENYA and UGANDA 1929-1933.—Plague has steadily diminished in both colonies. Much blame for the continuance of plague has been attached to the cotton industry inasmuch as the cotton grain is regarded as a food for rats. But it appears that only rats which are captured in a cotton district feed on this grain, while rats of other districts refuse it. The evidence on the connexion of the cotton industry and plague is not altogether convincing: insanitary conditions in the mills may be the real etiological factor. Destruction of rats is not favoured in either Kenya or Uganda as an effective plague measure either in town or country. Another important question which has been studied is that of the rôle of field rodents in the transmission of plague. The general opinion is that, "although in a rat epizootic some field rodents may be attacked, the majority of infected rodents belong to the species *Rattus rattus kijabius*." The plague problem of Uganda and Kenya is essentially one which is more rural than urban and depends on improvement of rural hygiene and material welfare.

As a vector of plague *Xenopsylla brasiliensis* is more important than *X. cheopis*. The latter flea infests rats of stone and brick buildings while the former is the flea of the hut.

W. F. H.

GOBERT (E.). Le rat alexandrin, commensal du paysan tunisien. [**The Alexandrine Rat a Commensal of the Tunisian Peasant.**]—*Arch. Inst. Pasteur de Tunis*. 1935. Apr. Vol. 24. No. 2. pp. 360–367. With 2 figs.

To the south and in the centre of the Regency of Tunis there has occurred between 1920 and 1931 an almost uninterrupted series of epidemic explosions of plague. The epidemics do not attack the built-up villages but are observed among the nomads or isolated peasants. It was this fact which led to the suspicion here of a connexion between the gerbil family of rodents and plague. Experiments, however, on this point have shown that this rodent, which is much the most prevalent, is much less susceptible to plague than other Tunisian rodents and shows no tendency to chronic plague. In the present investigation the fact emerges that it is *R. alexandrinus*, the domestic rat, living in close association with the Tunisian peasant, which is much more dangerous. It is the native rat, has been present for centuries, at least since the time of the Crusaders, and is the rat which has been captured almost exclusively outside the towns. The damage done by this rat is considerable. It lives not only on dates and fruits generally but also on the flower of the palm tree, which it seeks out before its emergence from the surrounding spathe. A regular poison campaign is conducted against this destructive rodent and nux vomica is used for the purpose.

W. F. H.

ESTRADE (F.). Observations relatives à la biologie de la *Xenopsylla cheopis* en Emyrne.* [**Biology of *X. cheopis* in Madagascar.**]—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 293–298. With 15 charts.

Experiments in Madagascar show that adults of *Xenopsylla cheopis*, among debris away from their host, survive longest at a temperature of 15°–20°C. and a relative humidity of 85–95 per cent.

The author's object was to relate the climatic conditions under which *X. cheopis* is most abundant and plague most liable to occur, with the experimental conditions under which these fleas can best survive apart from their host. The experiments were made in cement pits 80 cm. square, with debris from their normal haunts on the floor. The optimal conditions for survival were at a temperature of 15°–20°C. and a relative humidity of 85–95 per cent. Below 80 per cent. humidity at this temperature they lived only a few days. The higher the temperature the more sensitive they are to low humidity (because the saturation deficiency of the air is increased). These results, which agree very well with those obtained by LEESON (see this *Bulletin*, Vol. 29, p. 839) were confirmed by preliminary observations in nature at various altitudes in Madagascar, and they explain the seasonal incidence of plague in the Hauts-Plateaux, which is at a maximum in December and January.

V. B. Wigglesworth.

* Emyrne or Imerina appears to be that part of the plateau making up half of the island of Madagascar which lies around the capital, Antananarivo.

JAN-KERGUISTEL (A.). Répartition de la *Dynopsyllus lypusus* à Madagascar. [Distribution of *D. lypusus* in Madagascar.]—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 543–544.

ROUBAUD and MEZGER [*ante*, p. 449] have reported this flea, which can carry plague in Africa, not far from Antananarivo. Out of more than 50,000 fleas collected in 13 months in the Mahaiza sector there were only 44 specimens of *D. lypusus* 32 of which were on the rat and one on man. None of this species was present among 32,000 fleas collected in the highlands.
A. G. B.

KELLOGG (W. H.). The Plague Situation.—*Amer. Jl. Public Health.* 1935. Mar. Vol. 25. No. 3. pp. 319–322. [Summary appears also in *Bulletin of Hygiene*.]

After a note on the epidemiological aspects of plague the author sets out the record of plague in California since it was introduced into San Francisco about 1900. Two bubonic epidemics have been recorded, in 1900–04 and in 1907–8, and two small pneumonic epidemics in 1919 and 1924. In addition sporadic cases have occurred, mostly in rural districts and of squirrel origin, and squirrel plague has been found in 19 counties. The probability of plague dying out the author believes is small, for where a wild native animal such as the marmot has been the rodent concerned there is no evidence that the disease has ever completely disappeared. Such an endemic, and perhaps permanent, focus now exists in the California ground squirrel. A disquieting aspect is that whereas in rat plague pneumonia is not a common finding, in squirrel plague it is common. The Oakland outbreak (1919) of 13 pneumonic cases was started by contact with squirrels, the first man having been squirrel hunting just before onset. There is the possibility of direct extension of the disease in the wild rodent population across State lines, and recently plague has been discovered among the ground squirrels of Modoc County, 400 miles from the nearest previously known plague area and close to the State lines of Oregon and Nevada. It may also travel by transference to the rats in some border-line urban area, or by means of some person incubating the disease travelling east under the climatic conditions—low temperature with considerable humidity—that, it has been suggested, favour the spread of the pneumonic form.
A. Bradford Hill.

VOGEL (C. W.) & CADWALLADER (Charles). Rat-Flea Survey of the Port of Philadelphia, Pa.—*Public Health Rep.* 1935. July 26. Vol. 50. No. 30. pp. 952–957. With 1 fig.

A considerable number of vessels from plague infected ports call at Philadelphia. Many of these are not rat-proof and are laden with rat-attractive cargo. It is therefore important to take all suitable precautions to keep piers and water front in a rat-proof condition.

In the survey made the rat traps with rats, after being placed in bags, were taken to the laboratory and treated with hydrocyanic acid gas which enabled the operator readily to obtain the infesting fleas. Again, rats were chloroformed and combed for fleas over a well

illuminated white surface. All the rats were autopsied without discovering any with plague.

It was found that *X. cheopis* was essentially a rat-nest parasite and this accounted for its being found in the proximity of nests and on young rats. Altogether 2,765 rats were captured and these yielded 4,629 fleas. The main percentages according to species were:—*X. cheopis* 60, *Ceratophyllus fasciatus* 32, and *Ct. canis* (or *felis*) 2.6. Practically only one species of rat was encountered, *R. norvegicus*, and the *cheopis* index followed fairly closely the seasonal graph of relative humidity and temperature.

W. F. H.

TRIMBLE (H. E.) & SHERRARD (G. C.). **Rat and Rat-Flea Survey of Los Angeles Harbor.**—*Public Health Rep.* 1935 Jan. 18. Vol. 50. No. 3. 1 p. 74-79. With 1 fig.

This survey follows the usual lines. The most prevalent flea recorded was the mouse flea *Leptopsylla musculi* and the rat flea index generally was low. "In the writer's opinion the *Xenopsylla cheopis* index is too low to sustain an epidemic of rat plague." A common finding in such surveys as these is that the rat or the flea varies with the locality of trapping. In this case the *Leptopsylla musculi* index of rats increased "almost in direct ratio as the distance from the water front." This fact is partly accounted for by association of rats with mice: the mouse, and therefore its flea, is found in the open fields, which are unprotected from the sun and wind. The increase of the mouse flea upon rats was apparent especially on the rats caught in open country. As the ground squirrel in California has been reported to suffer from plague infection, a number of these were shot. They were found to be heavily infested with *Ceratophyllus acutus*, a flea which is a vector of plague for ground squirrels. Their flea index was 18.76 and this infestation would probably suffice to maintain foci of plague infection. None of the prevalent rat fleas, however, was found upon the squirrels.

W. F. H.

LONG (John D.). **Bubonic Plague on the West Coast of South America in 1934.**—*Public Health Rep.* 1935. July 19. Vol. 50. No. 29. pp. 923-932.

Some interesting facts have emerged in the course of co-operative antiplague work in Chile, Ecuador and Peru and are recorded in this report. In the routine inoculations for plague from rats trapped in Lima and Callao twelve guineapigs died from icterohaemorrhagic jaundice or Weil's disease. When the work of trapping was commenced, a large proportion of the rats was found to be suffering from abscesses especially in the liver and lungs; many of them, too, had helminthic infections, cysts in the liver and skin diseases. Since the rat population has been reduced through antiplague measures by about 60 to 70 per cent. in Lima and Callao, it is rare to meet with any of these conditions; possibly this is due to less opportunity for contact. Latent plague infection is not usually discoverable through any visible lesion. In these operations such infection was usually discovered only by making mass inoculations:—Small pieces of spleen and liver, occasionally lymph node, are taken from each rat that comes to autopsy and ground up with normal salt solution. Guineapigs are inoculated with

the resultant suspension by rubbing the smeared pestle over a scarified area on the belly of the animal. Some experiments were done with guineapigs which, although they had sickened, had not died of plague. No visible lesions of plague were discoverable in these animals and yet inoculation of organs in other guineapigs produced typical bubonic plague 30 days after recovery, in one case as late as 60 days and in another 90 days after.

Lice are not commonly incriminated as reservoirs of plague, but some of the experiments would seem to indicate that head lice may become infected with plague but are not capable of transmitting the disease. Two interesting outbreaks of human plague occurred in towns high up in the Andes, to which there are no roads and where there are no rats and therefore no possibility of an antecedent rat epizootic. These outbreaks are believed to have been due to infected fleas carried in the clothing and effects of mule drivers. The sequence of events in these cases was that the drivers picked up the fleas in towns at a lower altitude, where rats are numerous and plague, both human and rodent, is present. These drivers pass the night at inns located in the towns mentioned, sleeping on the floor, and guineapigs, which are commonly kept, "snuggle up against them for warmth . . . thus affording ample opportunity for mutual interchange of fleas." The first case of human plague, the first "that had occurred in the whole province in over 3 years" was in a woman who kept guineapigs. Her sickness and death were preceded by an epizootic among the guineapigs.

In his summary the author states his belief that "fleas under favorable conditions as to temperature and humidity, especially low temperature and relatively high humidities, can act as reservoirs of plague infection, carry it over long distances and later under favorable conditions transmit the disease. The incidents cited in this article strongly indicate that head lice and guineapig fleas can also act as reservoirs of plague infection and under certain special circumstances serve as the means by which plague infection is produced."

W. F. H.

RUDNEFF (George P.); TINKER (J.); KALABUCHOV (N.). **The Life Cycle of the Ground-Squirrel (*Citellus pygmaeus* Pall.), and the Laws of Development of the Plague Epizootic. II. Changes in the Leucocyte Picture of the Ground-Squirrel Blood in the Course of their Life Cycle** [RUDNEFF].—*Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 4. [In Russian pp. 291–297. [14 refs.] English summary p. 297]. **III. Changes in the Susceptibility of the Ground-Squirrels (*Citellus pygmaeus* Pall.) to the Plague in Connection with Sex and Age Differences** [TINKER & KALABUCHOV].—*Ibid.* [In Russian pp. 299–302. English summary p. 303.]

Rudneff has found that ground-squirrels during hibernation exhibit a leucopenia, with specially marked diminution of the neutrophils. To this fact he attributes the slow chronic course of plague and the maintenance of a reservoir of the plague virus in these animals during a non-epizootic period.

Tinker and Kalabuchov attempt to establish a correlation between the age and sex of ground-squirrels and their susceptibility to plague

infection. "The most susceptible are the young susliks born in the current year, then the adult females; the least susceptible are the adult males."

W. F. H.

WILLOUGHBY (W. M.). **Diagnostic and Other Experiences with Special Reference to Plague.**—*Jl. Roy. Nav. Med. Serv.* 1935. Apr. Vol. 21. No. 2. pp. 110–120.

Personal experiences by a former Port Medical Officer, which are related with graphic and humorous commentary, have a very special value for any one called upon to diagnose plague in the minimum of time. In the case of a ship the positive decision is very momentous for all concerned, including the Medical Officer. "A very good starting point for diagnosis of the human plague case is the finding or history of an associated dead rat." It is evident from the account given that the inspecting medical officer must likewise be alive to the possibilities of evasion of examination. The forms of the plague picture are distinctly variable and one rule to be followed is that, in the case of any one "at risk," even mild fever must be regarded as plague until the contrary is shown. Besides the actual history of the occurrence of dead rats the medical officer does well to enquire as to storekeepers. The rat, the food store and the storekeeper have, so to speak, somewhat close plague associations. Cases of plague seem to have a tendency to associate themselves with the storeroom. The storekeeper too is the man most likely to know of rat mortality on a ship. In the actual examination at "the muster" a port health officer becomes expert at picking out the man who is unwell and an expert at the detection of buboes in armpit or groin even through thick clothing and oil skins. It may also be his function to diagnose plague in the rat:—"The large spleen, marbled liver, pleurisy, peritonitis, petechiae and one or more haemorrhagic glands is a post-mortem picture of a rat dead of acute plague. More convincing still is an enlarged spleen . . . which yields the typical bipolar bacilli on film staining." One further observation may be useful to anyone in the circumstances here related. It is the resort to the flea comb for the rat with the recollection "that *Ceratophyllus fasciatus* has a very fine dog collar, denied, though not entirely, to the picture of *Xenopsylla cheopis*."

W. F. H.

GIRARD (G.). Vaccination de l'homme contre la peste au moyen de germes vivants (virus vaccin EV). Premiers résultats acquis à Madagascar. [**First Results in Madagascar of Vaccination of Man with Living Plague (EV).**].—*Bull. Acad. Méd.* 1935. July 2. 99th Year. 3rd Ser. Vol. 114. No. 25. pp. 16–22.

An account is given by the author of the use of living plague vaccine on a large scale after it was tested on a smaller scale. In so doing he makes return to one of the original methods of PASTEUR, as it was applied to anthrax, fowl cholera and swine erysipelas. The strain of plague bacillus (EV), which is avirulent, is constantly examined for the maintenance of its characters before use in the preparation of vaccines. In a country like Madagascar the procural of satisfactory statistical data is difficult but every endeavour has been made to obtain comparable figures. These figures are:—Vaccinated (46,879)—Deaths from plague 22 (0.47 per mille) and general mortality 225 (4.8 per mille). Unvaccinated controls (60,000)—Deaths from plague 100 (1.66 per mille) and general mortality 581 (9.7 per mille). W. F. H.

GOHAR (M. A.). **Protective Inoculation against Plague.**—*Jl. Egyptian Med. Assoc.* 1935. June. Vol. 18. No. 6. pp. 396-402. With 2 graphs.

A comparison is made between a killed (60°C., 1 hr.) vaccine, in which the endotoxin of the bacilli had been first liberated by repeated drying, grinding and resuspension, and vaccines in which the intact bacilli were killed by heat or by phenol. The experiment was carried out on guineapigs and rats and "the doses given were equivalent to 1,000, 2,000 and 5,000 million organisms injected subcutaneously in the thigh at weekly intervals." A minimum lethal dose was determined (1,000 million) for the living organism for the intraperitoneal route and the test dose was one of 8 M.L.D. Out of 48 guineapigs, divided into four groups of 12 each, one animal died in each of the batches immunized with killed intact bacilli and two in the batch of animals immunized with autolysed bacilli during the course of immunization. After injection of the test dose the animals were observed for 14 days. The results were:—survival of 2 animals out of 11 in the batch immunized with intact bacilli killed by heat, 3 out of 11 in the batch immunized with intact bacilli killed with phenol, 4 out of 10 in the batch immunized with autolysed bacilli, and none out of 12 in the control non-immunized batch. In the case of the rats the results were similar.

W. F. H.

BLANCHARD (M.), BLONDIN (P.) & ADVIER (M.). Septicémie pesteuse avec localisation oculaire suivie de guérison. [**Plague Septicaemia with Ocular Lesion followed by Cure.**—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 235-236.

This is a description of an unusual case of septicæmic plague with unusual local lesion. Grave general symptoms were present: continuous oscillating fever, rapid pulse, profuse sweating, asthenia, torpidity, low delirium, subicterus and painful hepatic enlargement. Malaria, relapsing fever, the typhoid fevers and abscess of the liver were each eliminated. Then came ocular symptoms: conjunctival redness, intense pain, diminution of vision and double hypopyon. At this moment, on the 10th day, blood culture, which had hitherto proved negative, became positive and the organism obtained was the plague bacillus. Anti-plague serum was administered, the symptoms cleared up rapidly and the patient left hospital cured one month after admission.

W. F. H.

PONS (R.). Au sujet de l'observation de septicémie pesteuse avec localisation oculaire suivie de guérison, rapportée par MM. M. Blanchard, P. Blandin et M. Advier. [**Plague Septicaemia with Ocular Lesion followed by Cure.**—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 354-356.

A description of a case of plague was given by BLANCHARD, BLONDIN and ADVIER which showed a trace of jaundice, enlargement of the liver, double hypopyon, blood culture positive only on the 10th day and final recovery. It is difficult to reconcile these facts. The author has found that blood cultures obtained from guineapigs, and contaminated with bacteriophage, show four periods of development—(1) A period of apparent sterility of 36 to 48 hours, (2) a period of only a few hours

duration during which the blood culture is feebly positive but cannot be subcultured on agar, (3) a new period of apparent sterility, which may last from 4 to 20 days, and (4) a period in which a new culture arises, more abundant, capable of subculture and phage-resistant. In these facts may be found the explanation of the case in question. The delay in blood culture would be due to the intervention of bacteriophage, while the jaundice and enlargement of the liver would be due to plague endotoxin set free by lysis of bacteria caused by specific bacteriophage.

W. F. H.

BONNE (C.). Over de pathologische anatomie der primaire longpest. [**Pathological Anatomy of Lung Plague.**—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1935. Apr. 2. Vol. 75. No. 7. pp. 564-571. With 2 figs. English summary.]

Two persons escaped from observation at Bandoeng in the hill region of Java, where plague is endemic and not infrequently pneumonic; decamped to Batavia; died there before their illness was recognized and were the cause within a few days of the development of plague pneumonia in three persons with whom they had come in contact. These three persons died of what was a primary pneumonia and not the form which is secondary to bubonic plague.

At the autopsy the pneumonia in two of these persons was found to be lobar and in the third to be largely oedematous but was to all appearance not very haemorrhagic. Lymph nodes at the hilum were enlarged, but again only slightly haemorrhagic. The other organs, too, except for slight bleeding under the epicardium, in the gastric mucosa and in the adrenals, were not obviously haemorrhagic. The haemorrhagic characters of the condition were much more apparent microscopically, but the feature which was most striking was the very large number of plague bacilli in the inflamed supporting tissue of the lung. Epithelium of the small bronchi was but little affected and remained in place. The deduction is made that a primary plague pneumonia can begin with an infection in the connective tissue and not necessarily as a bronchitis. In the pneumonic exudate there was but little fibrin present. One lobe was definitely involved throughout in pneumonia of the same stage and only small pneumonic areas were present in the other lobes. A noticeable feature in these three pneumonias was the comparative absence of a polymorph leucocytic reaction, as if the patients had died of an intoxication before this had time to take place. In none of the three cases was there a typical acute infection of the spleen.

W. F. H.

PIRIE (J. H. Harvey) & GRASSET (E.). **Concentrated Anti-Plague Serum.**—*Brit. Jl. Experim. Path.* 1935. Apr. Vol. 16. No. 2. pp. 126-128.

The method of concentration used was similar to that for anti-bacterial and other sera, a fractional precipitation process with sod. sulphate. A yield is obtained equal approximately to one-tenth of the original unconcentrated serum. Wild rats were used as test animals and the serum was inoculated intraperitoneally, while the testing dose of living plague bacilli was administered subcutaneously some time before, at the same time, or 24 hours after. One set of rats received concentrated serum, one set "ordinary" serum and one set no serum.

The minimum lethal dose of plague bacilli " was taken as the number which could be relied on regularly to kill a rat in 3 or at most 4 days." A number of the trials is set out for the exemplification of the results obtained, which went to show that the concentrated serum was four times as potent as the unconcentrated serum. W. F. H.

- DUPRAT. Peste bubonique et dératisation.—*Rev. Méd. et Hyg. Trop.* 1935. Mar.-Apr. Vol. 27. No. 2. pp. 57-78.
- FLU (P. C.). Immunisation des rats contre la peste au moyen de suspensions concentrées de bacilles pesteux virulents lysés par le bactériophage anti-pesteux. (2ième communication.)—*Acta Leidensia (Scholae Med. Tropicae)*. 1934. Vol. 9. pp. 1-20.
- JORGE (Ricardo). Regimento proveitoso contra ha pestenença—Lisboa, Valentim Fernandes 1496 (?).—Reprinted from *Rev. Clínica, Hig. e Hidrologia*. Lisbon. 1935. Jan. No 1. pp. 4-7.
- KELLOGG (W. H.). The Plague Situation.—*Amer. Jl. Public Health*. 1935. Mar. Vol. 25. No. 3. pp. 319-322.
- SCORRER (E. H.). The Deratisation of Ships.—*Jl. Roy. San. Inst.* 1935. Jan. Vol. 55. No. 7. pp. 380-387.
- SEYBERLICH (A.) & RANJEVA (J.). De la nécessité de l'examen des crachats dans un pays où la peste est endémique.—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 541-542.
- SILLEVAERTS (Ch.). La propagation de la peste, la dératisation et les idées nouvelles.—*Bruxelles-Méd.* 1935 June 9. Vol. 15. No. 32. pp. 880-884.
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LEPROSY.

LEPROSY REVIEW. 1935. July. Vol. 6. No. 3. pp. 100-148.
With 9 figs. on 4 plates. Quarterly Publication of the British
Empire Leprosy Relief Association, 131 Baker Street, London,
W.1. [2s.]

The first article in this number is on the oft described National Leprosarium of the United States by O. E. DENNEY. For approximately 500 patients 1,143,082 dollars have been spent on construction of the extensive buildings, including patients' quarters, infirmary, recreation building, school and library, administrative building, etc. The daily cost per patient is 2.39 dollars for 350 cases at present, and in fourteen years 801 patients have been admitted. This is the most completely equipped and staffed, and also the most costly, leper institution in the world.

Leprosy work in the Madras Presidency is dealt with by the medical officer in charge, J. J. JOSEPH, who points out that the leprosy survey of Dr. Santra in 1829 led to the organization of clinics for early out-patient treatment at low cost, of which there are now 400 working with yearly attendances of 903,090 in 1934 at a total cost of three lakhs of rupees (£22,500), in addition to which there are 2,100 inmates of leprosy institutions. An analysis of the results of treatment for three months and over at 107 of the clinics showed symptom free 5 per cent., greatly improved 33.5 per cent., slightly improved 40.5 per cent., leaving only 21 per cent. unimproved. A house-to-house survey in one area revealed 456 cases among 33,037 population, and the examination of 44,955 school students showed 483 cases, or 10.7 per cent. In 1930 56,000 were registered in the Province by the Public Health Department, but treatment at clinics has enabled about 120,000 to be registered. Due attention is paid to propaganda work and efforts to improve the local health conditions by visits and advice. The clinic attendances have more than doubled in two years and the treatment is becoming popular.

A comparative study of the efficacy of intradermal injections of ethyl hydnocarpate and ethyl morrhuate by G. R. RAO in a few selected cases, in which each drug was used on one side in symmetrical lesions, showed that the hydnocarpates were more effective both in reducing the lesions and the number of lepra bacilli in them, in spite of the morrhuate being the more irritant preparation; so it is concluded that the hydnocarpates have some special effect on both the cutaneous and the nerve lesions.

Leprosy in the Leeward and Windward Islands is reported on by R. G. COCHRANE. The Leeward Islands include Dominica, Antigua, Montserrat, St. Kitts and Nevis, of which Dominica and St. Kitts have the highest incidence, the last with a rate of 0.8 per cent., and it is noteworthy that in every case of nodular leprosy whose contacts were examined one to three children were found to have become infected. The Windward Islands include St. Vincent, St. Lucia and Grenada, and few cases were found in them. Throughout this area there was a close relationship between poor economical conditions and increased incidence and activity of leprosy, St. Kitts being a marked example of such a combination. Recommendations on the usual lines are made, and the provision of a central leper institute for all these small islands is discussed, but the danger of the removal of the patients far from their

homes leading to harmful hiding of cases is considered to be strong argument in favour of local arrangements. The remaining articles are reprints from other publications.

L. Rogers.

MONTAÑÉS (P.). **Leprosy in Spain.**—*Internat. Jl. Leprosy*. Manila. 1935. Apr.–June. Vol. 3. No. 2. pp. 197–200. With 2 figs. (1 map). Also in Spanish in *Medicina Países Cálidos*. Madrid. 1935. Sept. Vol. 8. No. 9. pp. 445–448. With 2 figs. (1 map).

In 1934 the author collected data of 928 cases of leprosy among the twenty-four million people of Spain, or nearly 0.04 per mille, but he estimated the cases at not less than 2,000, of whom 486, or barely 25 per cent., are hospitalized. The principal foci are in the Levante, Andalusia, Gallego and the Canary Islands. A recent regulation permits isolation of bacteriologically negative cases in their homes, and dread of the disease leads to notification and isolation of many cases, while open ones can be confined in leprosaria in Alicante and near Barcelona, where there is accommodation for 400 cases, which could easily be doubled. Chaulmoogra esters and hydnocarpates are used in treatment, together with local applications. Pyramidon is said to give surprising results in the control of reactions. In the last twenty-five years only 6.7 per cent. of some 893 Fontilles cases have been released as socially cured without relapse, most of those admitted having been in a very advanced stage. Better results are hoped for from treatment at venereal clinics under the recent decree, especially if early cases are sought for by epidemiological surveys, for "the efficacy of the treatment is beyond doubt."

L. R.

OTEIZA Y SETIÉN (Alberto) & TIAN Y DEL RÍO (Francisco R.). El grave problema de la lepra en Cuba. [**The Problem of Leprosy in Cuba.**]—*Vida Nueva*. 1935. June 15. Vol. 35. No. 6. pp. 301–370. With 12 figs., 1 diagram & 1 chart. [56 refs.]

This is a long article, half of it digressing into questions irrelevant to the title. The numbers of deaths from leprosy are given in two tables, showing those occurring in Havana itself and those in the interior. From 1902–1916 deaths at the Rincón leprosarium are included; the greatest number was in 1911 when 31 deaths occurred in the capital and 53 outside, or 9.5 per 100,000 inhabitants; in 1916 the figures were only 18 and 33 or 5.2 per 100,000, the lowest since 1910. Subsequent to 1916 deaths in the leprosarium were excluded and deaths in the city have never exceeded three and in the interior 47; in the last two years, 1931 and 1932, there was only one each year in the town and 30 outside, a rate of 0.18 per 100,000.

In June 1932 an enquiry was started in the Dermatological Division of the Mercedes Hospital and 23 cases were detected, 18 men and 5 women; 20 were of the nodular form, 3 of the nervous; 19 were Cubans, 4 were foreigners. The preponderance of the nodular type is shown also in the Rincón leprosarium records, 278 out of 387.

The authors interrupt the thread of their article by a digression into the history of leprosy prophylaxis from Babylonian times and accounts of what is and has been done in other countries all over the world. They proceed to apply the knowledge to their own country and to detail the need for compulsory notification, segregation under

special conditions ; treatment ; propaganda and educational measures ; epidemiological control, the question of marriage of lepers and the care of their children, and, finally, legislative measures, the clauses of a projected enactment being detailed. These are on the usual lines and do not call for comment.

H. H. S.

DINIZ (Orestes). Notas sobre a epidemiologia da lepra familiar em Minas Geraes. [**Epidemiology of Family Leprosy in Minas Geraes.**]*—Brasil-Medico.* 1935. June 15. Vol. 49. No. 24. pp. 531-534.

A list of 525 lepers registered in Colonia Santa Izabel in 1932 forms the subject of this study. Of these 207 or 39·4 per cent. attributed the infection to leprous relatives with whom they lived ; 84 or 16 per cent. habitually visited lepers living in the neighbourhood ; 19 or 3·6 shared rooms or came into close contact with cases ; 17 (3·2) vouchsafed the information that they lived near dwellings inhabited by lepers ; 4 said that they occupied houses in which lepers had previously lived ; 192 or 36·5 per cent. could give no reliable information as to the source. [These together total 523.] Attempt is made to determine the relative frequencies of infection from residence with kinsfolk, *e.g.*, from mother or father to son or daughter, uncles and aunts to nephews and nieces, brother to sister, etc., but the individual numbers of these so grouped are too small to be of much statistical value.

H. H. S.

PEREIRA (Paulo Cerqueira R.). Contribuição ao estudo da reacção de Bargehr—Allergia e imunidade activa contra a lepra. [**Bargehr's Reaction and Leprosy.**]*—Brasil-Medico.* 1935. June 29. Vol. 49. No. 26. pp. 576-587. With 6 figs. [18 refs.]

Bargehr's "Lepromine" is prepared from localized lepromata by cutting them into small pieces, heating them with a little water in a waterbath for 20 minutes to obtain a paste and to this is added phenol to 0·5 per cent. It is used in the same way as tuberculin in the von Pirquet test. As a result of his investigations the author has reached the following conclusions :—

1. The lepromine reaction is negative in children up to 2-3 years of age, as they are susceptible to infection.
2. Repeated inoculations transform the negative into a positive reaction and this is proportional to the number of injections.
3. Persons harbouring the bacilli and developing the disease react positively.
4. A positive reaction is probably due to antibodies resulting from contact with Hansen's bacillus.
5. A positive reaction with absence of symptoms in a person in constant contact with lepers denotes allergy and probable immunity.

In brief the findings are analogous with those of von Pirquet in the tuberculous and others exposed to infection.

H. H. S.

LEPROSY IN INDIA. 1935. Apr. Vol. 7. No. 2. pp. 57-108. With 2 figs. & 1 plate. Issued quarterly by the Indian Council of the British Empire Leprosy Relief Association.

The prognosis in leprosy is dealt with by Dr. E. MUIR in a valuable article which should be read in the original. He emphasizes the natural resistance of healthy adults, the great susceptibility of children, and the effect of small infections in producing acquired immunity.

The value of the leprolin test and the rapidity of red corpuscle sedimentation in estimating the resisting power of patients is next dealt with. He advises that the disease should have remained quiescent for two years before it is considered to be arrested and the patient watched for several years until the reaction to Hansen leprolin becomes stronger than that to Stefansky leprolin. In resistant cases the necessary period of treatment and observation is much shorter. The loss of thickening of the affected skin, reduction in the size and tenderness of nerves and in the extent of anaesthesia are favourable signs.

J. RODRIGUEZ records results of leprosy treatment at different age periods at the children's treatment station in the Philippines with chaulmoogra preparations in bacteriologically positive cases. At the age of puberty between 13 and 17 years the results were less satisfactory than before or after, for the relapses were 58.7 per cent. at that period against 49 and 48 per cent. respectively at earlier and later ages. He also considers that relapses at or before the age of puberty are more difficult to control than at later ages.

G. R. RAO reports on the leprolin test in early cases. He finds that purely neural cases without active symptoms show a fairly strong reaction to Hansen leprolin, indicating resistance, and these may then be considered "symptom free" or "arrested cases," but if nerve cases show a stronger reaction to Stefansky than to Hansen leprolin they may be considered to be potential cutaneous bacterially positive cases. K. BHATTACHARJI deals with the same subject and states that a positive leprolin reaction consists in the formation of a small nodule at the site of injection after two to four weeks. The higher the resisting powers of the patient the stronger will be the Hansen reaction, and *vice versa*, so the test may be of value in regulating treatment.

The other contents of this number are of local interest, such as a successful leper day in Bihar and local reports of clinics, etc. L. R.

BUITELAAR (L.). *Lepra onder de Sa'dan-Toradja's. [Leprosy among the Sa'dan-Toradjas.]—Geneesk. Tijdschr. v. Nederl.-Indië.* 1935. July 22. Vol. 75. No. 15. pp. 1211-1222. With 4 figs. on 2 plates.

In this article the author, on his own statement, does not claim to have brought forward any new facts or theories. It is simply the record of an investigation among a primitive people of the Island of Celebes. His object in making the investigation was to pave the way for setting up a leper hospital. The Toradja people, who are here concerned, number 191,000; their food is rice with a sufficient vitamin content, green vegetables and fish, but very little meat. Clothing and housing are of simple type, as also are the sleeping and the sanitary arrangements. The Toradja man is quite aware that infection occurs by personal contact, although he also believes in water-borne transmission. In some parts the married persons desert one another upon the onset of leprosy, but not in others. Of 185 lepers of marriageable age it was found that 77 were married, 21 unmarried, 67 separated and 20 were widows. The author discovered 204 lepers in 19 districts with a total of 163,288 inhabitants, but considers that the real total would be at least three times this number or, all over, about $3\frac{1}{2}$ per mille. The age distribution of these lepers worked out at 6-15 years 2 per cent., 16-25 years 10 per cent., 26-35 years 24 per cent. and 36 years or over 64 per cent. A bacteriological examination of 115 cases of pure skin

leprosy showed that the positive percentages were, for nasal mucosa, exudative serum and thick blood drop 80, 68 and 28 respectively and that by one or other method a positive result was obtained for 101 out of the 115. An unusually high positive result was also obtained for cases of nerve leprosy—23, 12 and 5 per cent. in the examinations of nasal mucosa, exudative serum and thick blood drop respectively. The question of infection by contact was investigated in 194 persons giving the figures 35, 27 and 38 per cent. for contact with family members, strangers and no known person respectively. A still more specific enquiry furnished the unexpected result that infection was traceable in greater degree to the father than the mother of a family. In the course of his tour, which was only of the nature of survey, the author took the opportunity, as a method of propaganda, to treat all lepers with one injection of ethyl ester and a handful of chaulmoogra pills.

W. F. Harvey.

HUIZENGA (Lee S.). **History of Leprosy in China.**—*Reports National Quarantine Service*. Shanghai, China. 1934. Ser. 5. pp. 89–108. With 1 map. [15 refs.]

Evidence is given in this note that leprosy was probably present in China 5,000 years ago in the time of Confucius, while a good description of the disease is on record in a work of about 610 A.D.

L. R.

WILSON (R. M.). **Sterilization and Marriage of Lepers.**—*Internat. Jl. Leprosy*. Manila. 1935. Apr.–June. Vol. 3. No. 2. pp. 201–204.

Owing to the separation of the sexes and prohibition of marriage in leper institutions many illegitimate children are born and become very liable to infection. Further, many suitable cases refuse to stay in institutions if not allowed to marry, but live a married life in camps and have many children, half of whom contract leprosy from their parents thus perpetuating the disease. To meet this very serious difficulty a self-supporting colony has been started by the author at the Korea Leper Colony under his charge by allowing couples to marry after the male partner has been sterilized by the very simple operation of vasectomy, but they are allowed to adopt a child from the colony, as the desire of Koreans to have a son is almost a religion. Help is given to enable them to build a house with land to cultivate, and at the end of a year's trial the experiment was working most successfully and the cost of maintenance of the couples was only one-fourth of the average.

L. R.

JIMENEZ RIVERO (Miguel). La intredermoreacción a la histamina en el diagnostico precoz de las manchas leprosas. [**The Intradermal Histamine Test in the Early Diagnosis of Macular Leprosy.**]—*Gac. Med. de Caracas*. 1935. Feb. 28. Vol. 42. No. 4. pp. 55–60.

The later stages of maculo-anaesthetic leprosy are usually diagnosed without difficulty. Far otherwise may it be in the early stages, with possibly atypical lesions. The author tried the histamine method of Rodriguez and Plantilla on early cases. Histamine is a vasodilator and its action depends on this. The effects of intradermal injection of

0.1 cc. are first the production of a local erythema appearing in 15–20 seconds; then a papule, raised and oedematous, and causing localized anaesthesia in 2–3 minutes, and thirdly, if the nerve-twigs are intact, a reflex erythema at the periphery of the oedema, which recedes after a few minutes.

In macular leprosy, in a minute or so after injection a small papule with oedema appears 1–2 millimetres in diameter, and increasing to its maximum of 1 cm. in five minutes, but without itching and without any erythematous halo. This is the important feature or, more strictly, its absence constitutes the importance of the test, for in the healthy skin there develops a reddish halo 1–4 cm. in diameter in 30–60 seconds, then a papule with itching, like that following a mosquito bite, lasting for $\frac{1}{4}$ –1 hour.

If the reaction is positive, *i.e.*, erythema, papule, oedema up to 1 cm. only, no itching and no red halo, the inference can be drawn that the bacilli have invaded the nerve endings, causing their degeneration, and that the macular patch is undoubtedly leprous.

The author gives brief notes of 13 cases so tested at the Asylum of Cabo Blanco.

H. H. S.

HOFFMANN (W. H.). Los gránulos intracelulares del virus de la lepra.

[**Intracellular Granules in Leprosy.**]—Reprinted from *Rev. Med. y Cirug. Habana*. 1935. Vol. 39. No. 11. pp. 709–718.

A child of 11 years suffering from leprosy came under the observation of the author. In stained smears of the secretion of superficial lesions of the hand he noticed small acid fast granules in the cytoplasm of leucocytes, although he did not meet with typical forms of the lepra bacillus. These granules were less acid fast than the bacillus and the author regards them as young forms or an early stage of the typical organism which have not the acid fast property fully developed. They were all of the same size and form and not merely (so he maintains) phagocytosed fragments of disintegrating bacilli, but examples of intracellular proliferation of young forms of the organisms—an intracellular phase in the evolutionary cycle of *Myco. leprae*. They are, he states, diagnostic of leprosy and are of great value in cases in which the grown organism is not found. He is of the opinion that the frequent failures at cultivation of Hansen's bacillus are ascribable to the fact that investigators have started with the adult, fully grown or degenerating forms instead of with these young, granular, developing forms. He accounts for the long latent incubation period of leprosy by suggesting that the intraleucocytic proliferation influences antibody production.

H. H. S.

MOSTERT (H. v. R.). **Leprosy : Some Aspects of Modern Research.**—

South African Med. Jl. 1935. July 13. Vol. 9. No. 13. pp. 459–463. [21 refs.]

This is mainly an historical and general consideration of the leprosy problem at the present day, but contains some South African experience. Thus, he records that the probable source of infection was traced in 372 cases, of which 64 per cent. were house infective and all the remaining 36 per cent. gave a history of previous close association with a leper. The age factor is illustrated by the fact that 230 (54 per cent.) of 426 children of lepers contracted the disease, and 78 per cent. of all

infections occurred before the age of 20 ; the parents suffering from the nodular type in 59 per cent. Among 385 married lepers, 43 per cent. being nodular cases, only 33, or 8.6 per cent., gave a history of conjugal infection after marriage with a leper. Hydnocarpus preparations are advised in treatment ; trypan blue was found to be too toxic, although more effective than methylene blue or brilliant green. L. R.

ARAGÃO (Henrique de Beaurepaire). Tentativas da inoculação de lepra humana em Didelphideos. [**Attempts to infect Opossums with Human Leprosy.**].—*Brasil-Medico*. 1935. Mar. 23. Vol. 49. No. 12. pp. 267–268.

This investigation was the outcome of a statement by Boyé in 1931 that he had seen in Cayenne an opossum (*Philander cancrivorus*?) an animal common in human dwellings there, with lesions resembling those of leprosy—emaciation, loss of skin in patches, and absence by amputation of terminal phalanges (see this *Bulletin*, Vol. 29, p. 270). Examination revealed enlarged glands in different parts of the body, the inguinal containing acid fast bacilli in groups of 4–8.

The authors have inoculated 55 opossums, *Didelphis aurita*, the commonest species in Rio de Janeiro, with fragments of leproma, with emulsions of leproma, or pus rich in Hansen's bacilli. Forty-seven were inoculated subcutaneously, five intraperitoneally, and one each via the pleura, the nose and into a bone. They can find no evidence of a special sensitivity of the opossum to leprosy, though the inoculated organisms persist for a long time, six months, and may perhaps show in greater number than appeared to be present in the original leproma. No difference was observed whether adults or quite young animals were employed. H. H. S.

MAXWELL (James L.). **The Treatment of Leprosy from a Public Health Point of View.**—*Chinese Med. Jl.* 1935. Apr. Vol. 49. No. 4. pp. 313–324.

The problem of leprosy in China, with possibly a million lepers, is dealt with from the public health point of view. The resemblance of leprosy to tuberculosis in its tendency to relapse is emphasized and its unsuitability for segregation measures on account of its slight infectivity, and long incubation and course, as well as the prohibitive cost is pointed out. Moreover, preventive inoculation is not possible at present. In Kwangtung a moderate estimate places the lepers at 200,000, whose segregation would cost a capital expenditure of twenty million and an annual one of twenty-four million dollars, while compulsory measures would hinder effective leprosy work by causing hiding of cases suitable for treatment. Education methods, especially in the medical schools, are required and information to lepers of the possibility of cure. The disease is essentially a rural one, from whence many go to the cities, so it must be attacked at its source. For this purpose the author advocates village clinics on the lines of the successful outpatient work of Dr. Fraser of Swatow, where within two months of its opening 92 patients were enrolled, mostly early cases, and almost without exception improvement resulted in a short time at a cost of

not more than one dollar per month each. A nurse should follow up the cases to their homes and advise preventive measures against infection. Voluntary settlements for advanced infectious cases are also of value, but when early treatment is generally available the very existence of advanced cases will in future be looked upon as a disgrace to the medical profession.

L. R.

LOEWENSTEIN (E.). Die Bekämpfung der Lepra auf Grund der neuesten Forschung. [**The Campaign against Leprosy.**].—*Wien. Klin. Woch.* 1935. Apr. 26. Vol. 48. No. 17. pp. 519-523.

This general account of the struggle against leprosy contains nothing new. The author estimates the world's lepers at 4,000,000. He once more emphasizes the diagnostic importance of finding lepra bacilli in the blood.

L. R.

SUSSINI (Miguel), ROBERTO PASO (Juan) & PUENTE (José J.). Organización de la lucha antileprosa en la República Argentina. [**The Leprosy Campaign in the Argentine Republic.**].—*Semana Méd.* 1935. May 9. Vol. 42. No. 19 (2156). pp. 1335-1342. With 1 map & 4 figs.

The number of lepers recorded at the National Department of Hygiene is increasing; in 1906 there were 724, in 1934, 2,959; of these 621 are in Santa Fe, 614 in Capital Federal, 339 in Corrientes, 317 in Buenos Aires and 297 in Córdoba. In short 88 per cent. of the cases are in littoral provinces, 11 in the central provinces and only about 1 per cent. in the mountainous districts. It must be borne in mind that this figure of 2,959 represents those actually known to the Health Department; there are others seen by medical men but not notified, others are under no medical care, others have been wrongly diagnosed, and the above total is therefore only indicative of the true prevalence which is very probably double or treble this.

The usual lines are laid down for dealing with the problem, according as the cases are in an early or advanced stage—the erection of dispensaries, establishment of leper colonies. Detailed general plans of such a colony are among the illustrations, others depicting a perspective view of the whole, and plans of the administration and treatment blocks. The general plan would be instructive, but unfortunately is printed too faintly for reproduction [incidentally it has been printed upside down]. That of the perspective view is good, but without the other cannot be interpreted.

H. H. S.

LEFROU (G.) & DES ESSARTS (J. Quérangal). Le problème de la lèpre tuberculoïde: premier et second mémoires. [**Tuberculoid Leprosy.**].—*Bull. Soc. Path. Exot.* 1935. Apr. 10. Vol. 28. No. 4. pp. 301-316. [14 refs.]

This paper describes some cases of tuberculoid leprosy and discusses the condition. After referring to earlier literature the author states that cases can only be recognized by microscopical examinations showing the special giant celled structure with few or no lepra bacilli.

L. R.

WADE (H. W.). **Tuberculoid Changes in Leprosy. IV. Classification of Tuberculoid Leprosy.**—*Internat. Jl. Leprosy*. Manila. 1935. Apr.–June. Vol. 3. No. 2. pp. 121–136. With 1 fig. [26 refs.]

The difficulty in classifying the tuberculoid form of leprosy is discussed, and it is pointed out that it was not dealt with in that recommended by the Memorial Conference in Manila, as the author only met with cases in a subsequent world tour in Japan, South Africa and India. He goes on to consider Japanese objections to the Manila classification, where tuberculoid cases are classed as a type of the macular form, and in South Africa as maculo-anaesthetic. The cases are benign and favourable with negative bacteriological findings, and histologically show non-lepromatous lesions with an extraordinary degree of reaction to the very few bacilli present. It is therefore considered that they should be classed as neural in a special sub-type to be indicated by the symbol Nt.

L. R.

HARROWER (Gordon). **Ainhum Disease and the Anaesthetic Type of Leprosy.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. June 29. Vol. 29. No. 1. pp. 73–76. With 3 figs.

The author records cases of ainhum somewhat resembling nerve leprosy.

L. R.

LARA (C. B.) & DE VERA (B.). **Early Leprosy in Infants born of Leprous Parents ; with Report of Cases.**—*Jl. Philippine Islands Med. Assoc.* 1935. May. Vol. 15. No. 5. pp. 252–260. With 4 plates.

Five cases of very early lesions in the children of lepers are described. In ten consecutive such cases seen at Culion in seven years a leprotic papule was observed in seven at ages between 15 months to 5½ years, and in the other three a reddish slightly raised macule was first noted, all being positive bacteriologically. In five of the ten cases two to six lesions were found simultaneously, but not grouped together. The papules were from the size of a pin's head to 2 to 3 millimetres in diameter, slightly flattened and fairly sharply defined. These early lesions tended to subside spontaneously, but resolved somewhat more rapidly under antileprotic treatment. Photos of some of the cases are published.

L. R.

RIBEIRO (Léonidio). **La lèpre est capable d'altérer les dessins papillaires des empreintes digitales. [Changes in Finger Prints due to Leprosy.]**—*Internat. Jl. Leprosy*. Manila. 1935. Apr.–June. Vol. 3. No. 2. pp. 195–196. With 8 figs. on 2 plates.

Illustrations are reproduced to demonstrate that leprosy lesions are able to produce complete alterations in the finger-prints of patients whose prints were available before their illness. Microscopical examinations showed that the changes were not due to atrophy, but to active lepromatous infiltration with the presence of lepra bacilli.

L. R.

ITAKURA (Teiju). Zahnärztliche Untersuchungen bei Leprakranken. II. Bericht: Klinische Untersuchungen ueber Pyorrhoea alveolaris bei leprakranken Formosachinesen (Fokien-Stamm). [**Pyorrhoea in Leprosy.**—*Taiwan Igakkai Zasshi* (Jl. Med. Assoc. Formosa). 1935. June. No. 6 (363). [In Japanese. pp. 827-834. German summary p. 835. 23 refs.]

This brief note records that pyorrhoea was met with in 52 per cent. of leprosy cases, and was more common in nodular than in nerve cases and in women than in men. It was also more frequent in lepers than in non-lepers.

L. R.

LAMPE (P. H. J.) & DE MOOR (C. E.). Ratten-lepra. [**Rat Leprosy.**—*Geneesk. Tijdschr. v. Nederl.-Indië*. 1935. Apr. 16. Vol. 75. No. 8. pp. 634-654. With 7 figs. on 2 plates. English summary.

The authors report their observations on rat leprosy in the Dutch East Indies. The diagnosis must be based on bacteriological examinations of the lymph nodes, which they have done in 5,000 trapped rats with from 5 to 25 per cent. positive results in different species of rats, the highest being in *R. concolor* and *R. norvegicus*. In 185 out of 500 naturally infected rats only the glands were involved, 10 per cent. of them showing many large colonies of bacilli. Superficial skin lesions were noted in 14 animals, so they regard the disease as a latent, but progressive one. The geographical distribution shows the disease to be world-wide if carefully sought for, and they suggest that what was originally a common saprophyte has secondarily adapted itself to the animal kingdom.

L. R.

BADGER (L. F.) & SEBRELL (W. H.). **Leprosy. The Effect of a Vitamin B₁ Deficient Diet on the Incubation Period of Rat Leprosy.**—*Public Health Rep.* 1935. June 28. Vol. 50. No. 26. pp. 855-863.

"Four experiments have been conducted in which white rats on a vitamin B₁ deficient diet and rats on a control diet have been inoculated, subcutaneously, with rat leprosy.

"The incubation period of rat leprosy in the rats on the vitamin B₁ deficient diet was appreciably shorter than in the rats on the control diet.

"In two experiments, white rats on a vitamin B₁ deficient diet were inoculated, subcutaneously, with human leprosy material. Local lesions were produced which have continued to increase in size."

L. R.

DEMANEZ (Marie-Lucie). Recherches sur la lèpre murine et le bacille Duval 514. [**Rat Leprosy and Duval's Bacillus 514.**—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 31-37.

This paper first deals with the feeding of fish with the organs of rat leprosy with negative results as regards inducing infection of the fish, although acid-fast bacilli were found in the intestines one month after. Next, leprosy rats were infested with lice, and after the death of the rat healthy ones were placed in the jar, but although lice were found on them they did not become infected with rat leprosy. Other experiments confirmed previous work showing that the injection of acetone

extracts of tubercle bacilli rendered rabbits temporarily susceptible to rat leprosy. Lastly, the acid-fast bacillus of Duval 514 was found not to become infective to rabbits injected with acetone extracts of tubercle bacilli.

L. R.

PRUDHOMME (R. O.). Résistance des bacilles de Stéfansky aux rayons ultra-violets. [**Resistance of Stefansky's Bacillus to Ultra-Violet Rays.**—*C. R. Soc. Biol.* 1935. Vol. 119. No. 27. pp. 1328–1330.

The action of ultra-violet rays in destroying the vitality of Stefansky's rat leprosy bacillus has been tested, and irradiation by a vapour mercury lamp at a distance of 20 cm. for not less than two minutes was found to render them harmless on injection into rats.

L. R.

OHTAWARA (T.); KAWAMURA (M.); ICHIHARA (Tsuruo). Studium der Lepra. II. Mitteilung: Wie reagiert der Leprakranke auf die intrakutane Injektion von Rattenleprabazillen? [OHTAWARA & KAWAMURA].—*Zent. f. Bakt.* I. Abt. Orig. 1935. July 23. Vol. 134. No. 5/6. pp. 312–315. III. Mitteilung: Das Verhalten der Geschlechtsdrüsen den Rattenlepra-bazillen gegenüber. [**Bacilli of Rat Leprosy.**] [OHTAWARA & ICHIHARA].—*Ibid.* pp. 316–318.

These workers have studied the occurrence of rat leprosy bacilli in the genital glands, and they found in rats with skin leprosy lesions these glands to be infected in 40 per cent. of males and 45 per cent. of female animals, and when the lymph glands were involved by the disease the male sexual glands were bacteriologically positive in 75 per cent. and the female glands in 26 per cent. These data show less frequent involvement in rat than in human leprosy.

L. R.

WALKER (Ernest Linwood) & SWEENEY (Marion S.). **Cultivation of Facultative Acid-fast Bacteria from Filtrates of Rat Leprosy and of Human Leprosy.**—*Jl. Infect. Dis.* 1935. Mar.–Apr. Vol. 56. No. 2. pp. 97–100. [11 refs.]

After a brief account of earlier literature on the cultivation of acid-fast bacilli from filtrates of human and rat leprosy material the authors record their own experiments. Using emulsions of human leprosy material passed through a Berkefeld N candle, they obtained one positive culture of acid-fast bacilli out of two, and with similar rat leprosy material passed through Sitz, Berkefeld N and W, and Chamberland L₂ and L₃ filters at a pressure of about 20 cm. of mercury positive results were got in 17 out of 52 tests. They do not, however, consider that these results support the claims of Markianos and others of the existence of an "ultravirus" stage of the leprosy organism, for they had previously demonstrated that a few acid-fast bacilli may pass through such filters even when control tests show that *Chr. prodigiosum* is retained by them. They consider these results support their view that Hansen's bacillus may be a tissue stage of the several types of pleomorphic and facultative acid-fast bacteria that have been repeatedly cultivated from human leprosy.

L. R.

WATANABE (Yoshimasa). **Experimental Studies on Animals concerning Leprosy. Report II. Inoculation Tests with Human Leprosy (Part I).**—*Kitasato Arch. Experim. Med.* 1935. Apr. Vol. 12. No. 2. pp. 139–153.

Experimental inoculations of rats with human leprous tissue are recorded. Subcutaneous inoculations were followed by cellular and connective tissue formation, with some giant cells and acid-fast bacteria, but no lepra cells, but the nodules healed and the bacilli disappeared in 71 to 400 days. Intravenous inoculations produced no nodules or other changes. Eye inoculations produced only temporary inflammation and nodule formation without any leprose changes. The degree of reaction is in proportion to the amount of material injected. L. R.

HISAMOUCHI (Y.). **Early Tissue Reactions in the Lungs of Rabbits after Intravenous Injections of Acid-fast Bacilli. Part 5. Experiments with Dr. Ota's So-called Acid-fast Bacilli of Human Leprosy.**—*Jl. Oriental Med.* 1935. May. Vol. 22. No. 5. [In Japanese. English summary pp. 69–70.]

The early tissue reactions of the lung to intravenous injections of human lepra bacilli is reported on, Ota's so-called acid-fast bacilli of leprosy being used. After phagocytosis of the bacilli monocytes formed a tubercle with considerable thickening of the alveolar septa. After seven days the bacilli could not be obtained and after a month the tubercle was no longer recognizable. L. R.

MANALANG (C.). **The Pathogenesis, Etiology, Transmission and Epidemiology of Leprosy.**—Reprinted from *Rev. Filipina de Med. y Farmacia*. 1935. July. Vol. 26. No. 7. pp. 265–268.

In this note the author once more states his hypothesis that leprosy is caused by an invisible virus which later develops into acid-fast bacilli. L. R.

VAUDREMER (A.) & BRUN (C.). **La culture du bacille de Hansen. [Cultivation of Hansen's Bacillus.]**—*Bull. Acad. Méd.* 1935. June 25. 99th Year. 3rd Ser. Vol. 113. No. 24. pp. 905–914.

Seven years' work on the cultivation of the lepra bacillus is recorded. Media employed in cultivating the tubercle bacillus were used, with the addition of filtrates through Chamberland L3 bougies of cultures of *Aspergillus fumigatus*. Either dissected out sterile leproma or the blood of leper patients taken during a febrile attack were employed. Lepromas taken during such a febrile reaction gave positive cultures in four cases, but three taken during quiescence of the disease were negative. A piece of the spleen from a post-mortem on a leper 30 hours after death was also used. After 15 to 30 days a Gram-positive pseudomeningococcus appeared in the cultures, but it produced no signs of meningitis on intraspinal injection in rabbits, so it is regarded as a stage in the development of Hansen's bacillus, for it was succeeded by a stage of fine granular cyanophilic bacilli, and later by innumerable acid-fast bacilli, which in one case appeared as early as the third day,

although in the case of fragments of spleen it took five months to reach this stage. The present cultures vary in age from 10 months to four and a half years. The presence of glycerine is necessary to produce acid-fast bacilli. Endospores are described and are considered to be a resisting stage of the organism. Animal experiments with the cultures showed that they develop through the Gram-positive cyanophilic to an acid-fast stage in the blood of rats and in the spleen and mesenteric glands of monkeys. Agglutination of the organism was obtained with sera from three lepers, a slight reaction with a tuberculous case and negative results with those of seven controls. Further, the serum of lepers alone produced lysis of the cultures. L. R.

YUYAMA (Hiroyoshi). Ueber die histologische Untersuchung der Glykogenverteilung in der leprösen Haut, mit besonderer Berücksichtigung der Beziehung zwischen der Funktion der Schweissdrüsen und der Schwankung des Glykogens. [**Glycogen Researches.**]—*Japanese Jl. Dermat. & Urol.* 1935. June. Vol. 37. No. 6. [In Japanese pp. 811-886. With 4 coloured figs. on 2 plates. [69 refs.] German summary pp. 134-136.]

The author reports his histological researches on glycogen destruction in the skin of leprosy patients with special reference to the sweat glands. When the function of the sweat glands is increased the glycogen decreases in them, and he has investigated the amount of glycogen destruction in various stages of 103 leprosy patients. In the maculo-anaesthetic form in all stages he found no glycogen in the epidermis except in the prickle cells, and also none in the lepra cells and other leprosy parts. In nodular cases he found similar deficiency of glycogen, and in the nerve and leucodermic forms he found none in either the epidermis or other parts, including the sweat glands. L. R.

POOMAN (A.). Ueber die Blutlipase bei Leprösen. [**The Blood Lipase in Lepers.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Feb. Vol. 39. No. 2. pp. 70-74. [20 refs.]

The author concludes from his observations that the blood lipase is diminished in leprosy, but increases when the condition of the patient improves and decreases when the patient gets worse. Remedies that are effective against leprosy increase the blood lipase, estimations of which are valuable in controlling the results of methods of treatment. L. R.

LOMHOLT (Svend) & ENGELBRETH-HOLM (J.). Bemerkungen zum Aufsatz P. Parmakson: Ueber die eosinophilen Zellen im Blutbilde der Leprakranken (*Dermat. Wschr.* 1935, Nr. 10, S. 285). [**Eosinophile Count in Leprosy.**]—*Dermat. Woch.* 1935. May 11. Vol. 100. No. 19. pp. 541-542.

This brief note records that intravenous injections of antileprol were followed by a considerable rise of the eosinophile blood corpuscles to 64 per cent., but intramuscular injections only produced inconstant and weak eosinophile reactions. L. R.

BIER (Otto G.) & ARNOLD (Käte). Ueber die Serologie der Lepra. I. Die Spezifität und Sensibilität der Rubino-Reaktion Untersuchungen ueber den Mechanismus der Reaktion. II. Komplementbindung bei Lepra mit dem Tuberkulose-Antigen von Witebsky, Klingenstein und Kuhn. III. Die serologische Differentialdiagnose zwischen Syphilis und Lepra. [**Serum Reactions in Leprosy.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. June. Vol. 39. No. 6. pp. 231-236; 236-238; 238-241. [14 refs.]]

The authors arrive at the following conclusions from their serological studies. I. The Rubino reaction in 327 leprosy cases gave positive results in 29·3 per cent. of pure nerve cases, in 41·7 of the maculo-anæsthetic type, in 56·5 of mixed cases, in 66·6 of nodular and in 13·8 per cent. of incipient cases. In 945 control cases only 0·1 per cent. were positive. In mixed cases the proportion of reactions increases with degree of involvement of the skin and varies from 20-42 per cent. in C₁ to 50-67 per cent. in C₃ cases.

II. Complement fixation in leprosy with the tubercle antigen of Witebsky, Klingenstein and Kuhn furnishes reactions that are of considerable diagnostic value.

III. The serological differentiation between leprosy and syphilis is dealt with in this section, and the authors conclude that leprosy sera can give complement deviation with tubercle and streptothrix antigens. Complement deviation with Witebsky and Gomes antigens give with leprosy effective antigen reactions of the same kind as in tubercle.

L. R.

SOULE (M. H.). **The Wassermann Reaction and the Kahn Test in Leprosy.**—*Internat. Jl. Leprosy.* Manila. 1935. Apr.-June. Vol. 3. No. 2. pp. 181-194. [22 refs.]

"The sera of 615 patients with more or less advanced cutaneous leprosy, and 54 other cases with severe lepra reaction, were tested by both the Kolmer-Wassermann and the Kahn procedures for syphilis. The group had been carefully selected, and comprised only individuals whose clinical examinations and case histories failed to reveal evidence of syphilis or yaws.

"Of the 615 sera from cases without lepra reaction the Wassermann test gave 109 strongly positive and 5 positive, a total of 18·5 per cent., as compared with 121 strongly positive and 70 positive, a total of 31 per cent. reactors with the method of Kahn.

"Of the 54 sera of patients undergoing severe lepra reaction 18 were strongly positive and 1 positive with the Wassermann test, and 18 strongly positive with the Kahn, 35·2 per cent. and 33·4 per cent., respectively.

"This study adduces considerable evidence that leprosy *per se* is responsible for the positive reactions."

L. R.

STEIN (A. A.). **Lepa Reaction and Meteorotropism.**—*Internat. Jl. Leprosy.* Manila. 1935. Apr.-June. Vol. 3. No. 2. pp. 137-152. With 6 figs. [25 refs.]

"1. The occurrence of exacerbation of leprosy processes depends upon changes in the atmospheric conditions.

" 2. There is no relation between exacerbation and the annual or monthly temperatures, the barometric pressure, rainfall or winds.

" 3. Exacerbations occur in a region with the passage of ' variable layers ' of different systems (cyclones, anticyclones, etc.).

" 4. The greatest number of exacerbations (73 per cent. of my cases) occurred during the passage of cyclones and occluded cyclones.

" 5. The greatest number of exacerbations were observed during the passage of the warm front of cyclones (44 per cent.), and next the cold front (29 per cent.).

" 6. In cold seasons exacerbations prevail when the warm front sets in, and to the contrary in the warm season when the cold front passes.

" 7. Multiple cases of exacerbation are more numerous and appear more frequently in winter.

" 8. In stable weather only a small number of cases of exacerbation was observed (7 per cent.) ; they appeared only as isolated cases.

" 9. The exacerbations of leprous processes appear not only on the day the variable layer passes, but also on the previous day." L. R.

LAGROSA (M.) & IGNACIO (J.). **Observations on Some Effects of Intradermal Injection of Certain Esters of Different Degrees of Saturation.**—*Jl. Philippine Islands Med. Assoc.* 1935. Apr. Vol. 15. No. 4. pp. 220-222.

Intradermal injections were made in thirty selected cases with symmetrical lesions using moderately unsaturated *Hydnocarpus wightiana* esters, highly unsaturated cod-liver oil esters, slightly unsaturated olive oil esters and practically unsaturated ethyl stearate. Observations were continued for a year with clinical and bacteriological examinations at from one to two months' intervals. The results showed no definite relationship between the degree of unsaturation and the results, for with the hydnocarpus and cod-liver oil preparations all showed clinical improvement, with the olive-oil esters 72.8 per cent. improved and with ethyl stearate 80 per cent., while only 40 to 45 per cent. of control uninjected areas clinically improved. Bacteriologically the hydnocarpus esters showed most improvement, with ethyl stearate a close second, cod-liver oil a fair third, and very little advantage from the olive oil preparation as compared with the controls. Further evidence is thus furnished of the superiority of the *Hydnocarpus* preparations.

L. R.

LAGROSO (M.), TIONG (J. O.) & DISINI (D.). **Further Observations on the Course of the Anesthesia following Antileprotic Intradermal Injections.**—*Jl. Philippine Islands Med. Assoc.* 1935. June. Vol. 15. No. 6. pp. 312-318.

The authors confirm their previous experience of the beneficial effects of intradermal injections of iodized *Hydnocarpus wightiana* esters on the anaesthesia of leprosy. There was relatively greater proportionate improvement in treated than in control areas in twenty-five patients with symmetrical lesions, who were also given intramuscular injections of the drug, after eight months treatment followed by suspension for two or three months ; 88 per cent. of the treated improved against 52 per cent. of the control areas. Injections of ethyl oleate and normal saline showed 75 per cent. improved against 41 per cent.

of controls ; this is attributed to the mild trauma and irritation produced. A combination of subcutaneous, intramuscular and intradermal injection is advised. L. R.

KEIL (Ernst). Zur Behandlung der Lepra mit Jod-Antileprol. [**Treatment of Leprosy by Iodized Antileprol.**].—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. May. Vol. 39. No. 5. pp. 188-199. With 6 figs. [14 refs.]

The author deals with treatment by the iodized chaulmoogra esters first introduced by COLE in the Philippines, but he advocates the addition to the esters of 10 per cent. instead of $\frac{1}{2}$ per cent. iodine, and gives from $\frac{1}{2}$ to 3 cc. once or twice weekly, largely by the intradermal method. He warns that a rise of temperature or congestive dermal reactions are contraindications for continued treatment. Of 273 cases 110 were treated for over one year and 163 for over two years, and 20 per cent. were cutaneous, 57 neural and 23 per cent. mixed cases ; 21 per cent. were early, and 75 per cent. more advanced. The results were that 13 per cent. became negative bacteriologically, 44 showed clear improvement, 41 were stationary and 2 per cent. became worse. L. R.

GRIMES (Ch.), CLUZET & MINEC. Note préliminaire sur un essai de traitement de la lèpre à Madagascar par le violet de gentiane. [**Treatment of Leprosy with Gentian Violet.**].—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 415-416.

The authors report a trial of intravenous injections of 3 mgm. per kilo of gentian violet in 1 per cent. solution intravenously twice a week without any toxic symptoms. In 35 cases a series of 24 injections produced effects on the nerve symptoms in the form of healing of ulcers, diminution of paralysis of the hand muscles and of erythematous and depigmented patches, and of anaesthesia. It is too early to say if the effects will be lasting. L. R.

DELANOË (E.). Le bleu de méthylène compris dans le traitement mixte de la lèpre. [**Methylene-Blue in Leprosy.**].—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 348-353.

Two cases are recorded treated by injections of methylene blue. The staining of the leprous lesions is regarded as a valuable diagnostic aid in the case of hyperplastic lesions only, but the vitality of the lepra bacilli does not seem to have been impaired. M. MARCLOUX pointed out that the six injections used would not suffice to test the value of the dye. L. R.

FERNANDEZ (José M. M.) & SCHUJMAN (Salomón). El empleo de las anilinas en el tratamiento de la reacción leprosa. [**Aniline Dyes in the Treatment of the Leprous Reaction.**].—*Rev. Leprologia de São Paulo.* 1935. June. Vol. 2. No. 2. pp. 79-85.

MUIR and CHATTERJI have recommended the use of mercurochrome in cases with leprous reaction, and the authors have tested this, and fluorescin and eosin for the same condition.

Mercurochrome contains between 20 and 25 per cent. metallic mercury and also a certain proportion of fluorescin. It has been employed

as an antiseptic for a considerable time and in leprosy MUIR and CHATTERJI attribute a threefold action to it, (1) on concomitant sepsis, (2) on the allergic state, the leprous reaction, and (3) provoking necrosis and resolution of lepromata. The authors used a 1 per cent. solution in fresh distilled water, giving 3 cc. intravenously and 3-4 days later 5-8 cc. and thereafter 10 cc. weekly according to the degree of tolerance and the results obtained. Signs of intolerance are stomatitis, gastrointestinal disturbance, rise of temperature and sometimes shivering immediately following the first injection, but as a rule the drug is well tolerated. Of 16 patients so treated, 6 were greatly benefited, 4 partially, in 3 the result was doubtful, and in 3 its use failed altogether.

Fluorescein was used in doses of 10 cc. intravenously every 4 days, the strength of solution being 2 per cent. freshly prepared, filtered and sterilized. Eleven patients so treated showed perfect tolerance, but in 3 only who presented iritis or acute ocular symptoms of the leprous reaction did it succeed and in them the improvement was immediate.

The authors used eosin in a 2 per cent. strength in distilled water, 10 cc. intravenously every 4 days. Seven patients were treated but though none showed any signs of intolerance none received any benefit from it.

H. H. S.

TISSEUIL (J.). Essai de traitement de tuberculoïde de la lèpre par la crisalbine. [**Treatment of Tuberculoid Leprosy with Crisalbine.**]—*Bull. Soc. Path. Exot.* 1935. May 8. Vol. 28. No. 5. pp. 346-348. With 2 figs.

The author reports that although others have been unsuccessful in treating leprosy with gold preparations he has found crisalbine in a total amount of 5 gm. in two series of weekly 10 cgm. doses had a good effect in a tuberculoid case in which hyrganol had failed.

L. R.

DUBOIS (A.), WESTERLINCK (H.) & DEGOTTE (J.). Essais thérapeutiques dans la lèpre : le manganyl. [**Manganyl in the Treatment of Leprosy.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 19-23.

The author reports a trial of the manganese preparation Manganyl in 25 cgm. doses intravenously without toxic symptoms. One patient died under circumstances not determined. Three maculo-nervous and two nodular cases did not show any active results of the treatment, but larger doses will be tried.

L. R.

ROUSSEL (J. N.). **Leprosy : a Report of Twenty-Seven Cases treated with Anthrax Vaccine.**—*Jl. Trop. Med. & Hyg.* 1935. June 1. Vol. 38. No. 11. pp. 133-136. Also in *Southern Med. Jl.* 1935. Aug. Vol. 28. No. 8. pp. 730-735.

Seventeen maculo-anaesthetic and 9 nodular leprosy cases have been treated in New Orleans by a vaccine made in Philadelphia said to contain living attenuated spore-bearing anthrax bacilli, of which over 700 injections were given without ill effects. No improvement was noted in the nodular cases, but the nerve cases are said to have benefited in the way of fading of the lesions in two-thirds of them, commencing two or three months after the injections were stopped.

L. R.

SORLEY (J. T.). **The Use of Brilliant Green Intravenously in the Treatment of Leprosy.**—*West African Med. Jl.* 1934. Oct. Vol. 8. No. 2. pp. 13-14.

Brilliant green was given in much smaller and less toxic doses than used by G. A. RYRIE, namely 3 cc. of a 1 per cent. solution twice weekly for three months in 24 cases. No bacterial or sedimentation improvement was obtained, but there seemed to be considerable clinical improvement. L. R.

DE LA PLAZA (G.), VEGAS (M.) & GOMEZ (B.). La neurotoxina de Cascabel (*Crotalus terrificus*) en las alalias del brote nervioso en la lepra. [**The Treatment of Crises of Nervous Leprosy with Crotalus Toxin.**]—*Rev. Policlínica Caracas.* 1935. Apr. No. 21. pp. 137-1402.

[The term "crisis" (algia) is employed here in the same sense as in tabes dorsalis, for exacerbations of pain, neuritic, arthralgic, etc., such as occur in leprosy.] The neurotoxin of *Crotalus terrificus* was prepared in the National Laboratory and put up in 2 cc. ampoules each containing 0.1 mgm. in glycerin, and the remedy was employed in 30 cases. In 14 the result is described as excellent, and in another 14 there was improvement [presumably alleviation of pain], in two only did it fail, and in many the relief followed promptly on its administration. [We cannot find in the account any statement as to the mode of its use, whether injected subcutaneously, or along the affected nerve, or at the nerve root, although a brief note is given of each of the 30 cases.] H. H. S.

PRUDHOMME (R. O.). Fixation *in vivo* du bleu de méthylène par les bacilles lépreux. [**Fixation of Methylene Blue by Lepa Bacilli in vivo.**]—*C. R. Soc. Biol.* 1935. Vol. 119. No. 27. pp. 1326-1328.

The author reports finding that the potential oxido-reduction of lepromes is not materially different from that of normal tissues, and that the substances which fix methylene blue to lepra bacilli belong to a series of substances which can be extracted by hot alcohol. L. R.

PALDROCK (A.). Noch eine durch spezifische Behandlung geheilte Lepröse. [**Leprosy cured by specific Treatment.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. June. Vol. 39. No. 6. pp. 241-243. With 3 figs.

This author once more advocates the use of carbon dioxide snow locally and the injection intravenously of gold preparations in leprosy.

L. R.

OTA (Masao), SATO (Saburo) & MASUZAWA (Tatsuro). **A Chaulmoogra Preparation for Intravenous Use, and its Therapeutic Effect.**—*Internat. Jl. Leprosy.* Manila. 1935. Apr.-June. Vol. 3. No. 2. pp. 153-164. [28 refs.]

The authors report their work on a preparation of chaulmoogra for intravenous use. They have made fine emulsions of the ethyl esters about 1 micron in diameter in a stable colloidal state containing from

10 to 50 per cent. of esters, and have used a 40 per cent. emulsion, as a standard, although for production in quantity a 10 per cent. emulsion has been adopted and named "esperol." A dose of 0.5 cc. per kilo of the 40 per cent. solution caused no unpleasant symptoms in rabbits, and single doses of 2.5 to 3 cc. up to 5 cc. have been injected intravenously into patients, but they find it is much safer to dilute the emulsion five to ten times with distilled water, normal saline or 4.5 per cent. glucose solution. Up to a total of 50 injections amounting to 148 cc. of the standard 40 per cent. emulsion have been given to one patient. Further experience is required to determine the value of this method, but they are convinced that it is not inferior to others yet used. L. R.

FRASER (N. D.). **A Village Clinic for Leprosy Treatment.**—*Internat. Jl. Leprosy*. Manila. 1935. Apr.–June. Vol. 3. No. 2. pp. 204–206.

At the Swatow Mission Hospital in the Chinese province of Kwangtung over 1,000 cases of leprosy have been met with in six years and at least 10,000, or 5 per mille, are believed to be present in the district, of whom 100 are in a colony and 100 more attend a clinic. It was therefore decided to organize a village clinic with voluntary medical attendance, and by the end of the year about 100 patients were attending regularly for treatment, some coming ten to twenty miles for it. Iodized esters and alepol were used. The plan met with such success that other village clinics are to be started shortly. L. R.

CRUZ (M. C.). **Parenteral Administration of Fresh and Boiled Leprotic Emulsions in Lepers.**—*Jl. Philippine Islands Med. Assoc.* 1935. June. Vol. 15. No. 6. pp. 319–323.

In order to test if lepra reactions are caused by breaking down of numerous lepra bacilli, lepromata, some freshly ground, others boiled, were injected intravenously, intramuscularly and subcutaneously in lepers, but only very slight general reactions without anything like typical lepra reactions resulted, nor were any allergic reactions noted. L. R.

CRUZ (M. C.). **Trial of High Fat Diet and Fixation-Abscess in Lepra Reaction.**—*Jl. Philippine Islands Med. Assoc.* 1935. Apr. Vol. 15. No. 4. pp. 214–220.

The methods of treatment of lepra reaction are considered and the administration of sodium bicarbonate and calcium chloride are stated to be the best at present available. A high fat diet has been suggested with a view to increasing the blood lipoids, as they are found to be low in those who are worse after severe reactions. Fixation abscesses were also tried because occasionally remarkable improvement has followed severe suppurative reactions with hyperleucocytosis. Cod-liver oil, butter and eggs were given for the first purpose, and injections of a total of 13.5 to 40 cc. of a turpentine-oil mixture in from 4 to 12 doses for the second, with resulting increases of the total leucocyte count of from 400 to 13,500 over the initial count, but no material increase in the total blood lipoids followed the special diets. The results showed no advantage in lepra reactions over the control cases, so further study of such reactions is required. L. R.

DUBOIS (A.), WESTERLINCK (H.) & DEGOTTE (J.). Essais thérapeutiques dans la lèpre : le sulfate de cuivre. [**Sulphate of Copper in Leprosy.**].—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15. No. 1. pp. 25-29.

The treatment of 47 cases of leprosy by intravenous injections of copper sulphate in 0.25 to 0.5 per cent. solutions, and total doses of 3 to 5 gm. in the course of 4 to 7 months is reported, but negative results were obtained in cutaneous, macular with few bacilli and in maculo-nerve cases with rare bacilli. L. R.

SUMMENT (Peter). Klinische Betrachtungen ueber die Lepra und deren Behandlung. [**Observations on the Treatment of Leprosy.**].—*Dermat. Woch.* 1935. Aug. 17. Vol. 101. No. 33. pp. 1002-1006.

In this note the author records his general experience of leprosy in the Baltic area chiefly among the fishermen of the coast. He advocates the use of a tar sulphur powder for local application to ulcers.

L. R.

ARANTES (Luiz). Da gynecomastia da lepra.—*Brasil-Médico.* 1935. June 8. Vol. 49. No. 23. pp. 511-520. With 7 figs.

COCHRANE (Robert G.). Observations in the West Indies. [Correspondence].—*Internat. Jl. Leprosy.* Manila. 1935. Apr.-June Vol. 3. No. 2. pp. 228-229.

NITTIS (Savas). Prominence of the Right Sterno-Clavicular Junction as a Sign of Early Infection in Leprosy.—*Jl. Egyptian Med. Assoc.* 1935. June. Vol. 18. No. 6. pp. 403-412. With 6 figs.

POOMAN (A.). Eine zweckmässige Uebersichtsmethode der Leprabehandlung.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935 Jan. Vol. 39. No. 1. pp. 25-28.

PUBLIC HEALTH REPORTS. 1935. Mar. 29. Vol. 50. No. 13. pp. 442-444. —Observations on the Epidemiology of Leprosy in Hawaii.

RODRIGUEZ (J.) & PLANTILLA (F. C.). Observations on the Progress of "Incipient" or Early Lesions of Leprosy.—*Monthly Bull. Bureau of Health.* Manila. 1935. Mar. Vol. 15. No. 3. pp. 97-108. With 1 fig.

SCHLOSSBERGER (H.). Die Behandlung der Lepra und der Tuberkulose mit Chaulmoograöl.—Reprinted from *Zent. f. d. gesamte Tuberkuloseforsch.* Vol. 42. No. 9/10. pp. 545-576. [7 pages of refs.]

SOLANA (Federico) & GUTIÉRREZ-SOLANA. Sobre el cultivo "in vitro" del bacilo de Hansen.—*Medicina Paises Cálidos.* Madrid. 1935. Apr., May & June. Vol. 8. Nos. 4, 5 & 6. pp. 177-183; 233-246; 271-294. With 6 figs. [225 refs.]

THOMPSON (E. I.) & DE GROAT (A.). Macular Leprosy. Report of a Case occurring without Anesthesia.—*Jl. Amer. Med. Assoc.* 1935. Aug. 3. Vol. 105. No. 5. pp. 357-359. With 5 figs.

YELLOW FEVER.

- i. JAMES (S. P.). Renseignements concernant la fièvre jaune reçus pendant les 6 mois se terminant au 31 mars 1935. [**Information concerning Yellow Fever received during the 6 Months ending 31st March, 1935.**—*Bull. Office Internat. d'Hyg. Publique.* 1935. July. Vol. 27. No. 7. pp. 1312-1316.
- ii. BOYÉ. Les cas de fièvre jaune dans les colonies françaises en 1934. [**Cases of Yellow Fever in French Colonies during 1934.**]—*Ibid.* pp. 1317-1318. With 1 folding map.
- iii. —. La "fièvre rouge" congolaise et le test de protection amaril en Afrique équatoriale française. [**"Red Fever" of the Congo and the Yellow Fever Protection Test in French Equatorial Africa.**]—*Ibid.* pp. 1319-1321.
- iv. PRIDIE (E. D.). Recherches concernant la fièvre jaune au Soudan anglo-égyptien depuis octobre 1934. [**Researches concerning Yellow Fever in the Anglo-Egyptian Sudan since October, 1934.**]—*Ibid.* pp. 1322-1323.
- v. DE VOGEL (W. T.). Un bataillon soudanais en garnison dans un foyer de fièvre jaune. [**A Sudanese Battalion garrisoned in a Yellow Fever Centre.**]—*Ibid.* pp. 1324-1331. With 1 map.
- vi. SCHILLING (Claus). Sur la question des régions à fièvre jaune "silencieuses". [**The Problem of "Silent" Yellow Fever Regions.**]—*Ibid.* pp. 1332-1336.
- vii. JORGE (Ricardo). A propos de la fièvre jaune endémosporadique. [**Concerning Endemo-Sporadic Yellow Fever.**]—*Ibid.* pp. 1337-1341.
- viii. THEILER (Max) & WHITMAN (Loring). Le danger de la vaccination par le virus amaril neurotrope seul. [**The Danger of Vaccination by Neurotropic Yellow Fever Virus Alone.**]—*Ibid.* pp. 1342-1347.
- ix. BULLETIN DE L'OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1935. July. Vol. 27. No. 7. pp. 1348-1349. Rapport de la commission de la fièvre jaune. [**Report of the Yellow Fever Commission.**]

i. During this period cases of yellow fever have been recorded from Gambia, Gold Coast, Ivory Coast, Niger Territory, Nigeria and Sierra Leone, in Africa; from Matto Grosso and Goyaz in Brazil; and from Restrepo in Colombia. The most important outbreak is that in the State of Goyaz with more than 100 cases [*ante*, p. 586].

The results of further protection tests confirm its value as an indication of the occurrence of yellow fever in the past, and the majority of workers are now of the opinion that yellow fever is the only disease which gives a positive reaction, although Boyé [*infra*, p. 875] maintains the possibility of it being non-specific. The use of the viscerotome for obtaining specimens of liver for pathological examination has not been made compulsory in Africa, but instruments have been sent to most of the British colonies. The general epidemiology of the disease is next discussed with special reference to recent rural outbreaks in Brazil. The fact that hedgehogs are susceptible to the disease, and the occurrence of immune bodies against yellow fever in wild monkeys in Brazil, supports the view that vertebrate hosts other than man occasionally may serve as reservoirs of infection.

In England, combined virus and immune serum is used for vaccination against yellow fever. As a general rule heterologous immune

serum is used in doses of 0.4 to 0.5 cc. per kilo body weight, and the only inconvenience of such serum is that occasionally the inoculation is followed by severe urticaria and arthritis. The method has also been used in other parts of the world and it is noted that practically all the European residents in Gambia have been vaccinated, a very satisfactory result, in view of the great practical difficulties of dealing with endemic yellow fever in this Colony.

ii. During 1934, 23 cases of yellow fever with 19 deaths have been recorded from the Senegal, Ivory Coast and Niger Territory. The French Sudan and Guinea have had no cases this year. The distribution of these cases is given in a map, which also includes records of cases during the years 1931, 1932 and 1933. STANTON records that in British colonies during 1934 there was a total of 10 European and 9 native cases, including 5 suspected cases in Nigeria, Gold Coast and Gambia.

iii. The author records the experience of a medical officer, GRALL, in the Oubangui district of the Congo, who a few months later travelled through regions where BURKE had found that many of the natives gave positive protection tests against yellow fever. According to GRALL, many of these cases had suffered from an obscure disease known as "Red Fever of the Congo" (*Fièvre rouge congolaise*) and it is suggested that this infection may have been responsible for these positive results. The author calls attention to this disease, as he considers that the possibility of obtaining a positive protection test in the absence of yellow fever has not been finally excluded. [See below, p. 881.]

iv. The livers of seven doubtful cases in the Sudan were examined histologically by FINDLAY and two of them were considered suspect. One of these cases had a history of jaundice, 7 days fever, coma and death, but his serum gave a negative protection test. The examination by means of yellow fever protection tests of 43 sera from cases of jaundice resulted in 9 positives; 8 of these came from the south of the Sudan and the other from Wad Medani. The latter succumbed to an infection clinically resembling yellow fever, but sections of the liver were negative.

v. An interesting account of the medical history of the Sudanese battalion, recruited in Darfur and Kordofan, which was employed as a garrison from 1863 to 1867 at Vera Cruz during the Mexican war. The author has obtained his information from three military treatises on this expedition:—"*Mes souvenirs*," by General DU BARAIL; "*Cinq ans au Mexique*," 1862–1867, by ADRIEN DE TUCÉ; and "*L'expédition du Mexique* (1861–1869). *Récit politique et militaire*," by G. NIOX.

The observations in these treatises abundantly confirm the view to which Prince Omar Toussou first called attention [see this *Bulletin*, Vol. 31, p. 834], that these Sudanese were immune against yellow fever, and consequently must have been exposed to infection before their arrival in Mexico. These historical facts correspond with the results of recent protection tests and show that yellow fever must have existed in the Sudan for long periods. The reason why it has never spread to the East Coast of Africa is attributed by the author to the sparsity of the population between the infected Sudanese provinces and the coast.

vi. The author discusses the problem of the existence of a considerable percentage of the population giving positive protection tests against yellow fever in regions where clinical cases of the disease have never been observed. He refers to KLEINE's examination of 101 natives of East Africa [see this *Bulletin*, Vol. 27, p. 558] none of whom

gave a positive Schick reaction, although there was no evidence of previous exposure to diphtheria. Similarly a commission for the study of tuberculosis in mine labourers in South Africa found that approximately 72 per cent. of the natives gave a positive tuberculin reaction, although tuberculosis occupies a very small place among the diseases affecting the districts from which they were recruited.

Various hypotheses have been advanced to explain these facts, one being the existence of latent infections, such as those observed in many laboratory cases of yellow fever, where characteristic symptoms may be completely absent. The author insists on the necessity of a detailed examination of any doubtful febrile cases in endemic areas, and the use of the viscerotome for the examination of the liver in patients who have succumbed to any febrile disease within 10 days.

A second explanation is the possibility of non-specific reactions analogous to Forssmann's heterogenetic antigens and antibodies; or the para-agglutinations, such as that between *Proteus X 19* and serum containing typhus antibodies.

Another problem is whether a positive reaction against a virus that has been maintained by mouse passage, or in monkeys, necessarily signifies that the subject would be immune against virus inoculated by an infected mosquito. Similarly, where there is a high degree of latent infection is it possible for the virus to acquire a high degree of virulence? a point of considerable importance in view of the danger of the transport of infected mosquitoes by aeroplanes. With reference to protection the author considers the simultaneous injection of virus and immune serum as the method of choice. Animal reservoirs are considered to be of very secondary importance in the spread of the disease in view of the very sharply defined geographical limits of the disease.

vii. The author presents various observations on the epidemiology of yellow fever, with special reference to conditions in Brazil, where recent investigations [*ante*, p. 585], have shown that there are two kinds of endemicity, one urban, affecting mainly the coastal towns, and the other "hinterlandic" resulting in the appearance of scattered centres of infection in sparsely populated areas. Whereas in the Gulf of Mexico, the suppression of the urban type has resulted in the complete disappearance of yellow fever, in South America a number of rural centres of infection have been left behind.

After mentioning the efficiency of mosquito control in Brazil and the value of the viscerotome, the "mouse test" is discussed with special reference to its specificity. Attention is again drawn to the results of the Schick test for diphtheria among native populations where the disease is extremely rare or absent. In Nigeria, for example, out of 1,758 natives, 81 per cent. neutralized the toxin and in Morocco out of approximately 2,000 subjects only four gave a positive reaction. Similarly in the United States the disease is much commoner among the white population than among negroes, and among those the incidence diminishes as one goes south. In the Bahamas, out of 300 black children only 4 were carriers of Loeffler's bacillus, whilst 90 per cent. gave a negative Schick test. These racial peculiarities may possibly have some parallel in the case of yellow fever, where the natives, especially in America, seem to show a relative immunity against the disease.

viii. A valuable discussion of the method of vaccination by means of neurotropic yellow fever virus alone, as advocated by LAIGRET. The authors' experiments confirm those of FINDLAY [*ante*, p. 285], that inactive virus produces no effect, and that any

resulting immunity depends on the injection of living virus. Consequently this method involves the danger of the presence of a neurotropic virus in the circulation. The large number of persons vaccinated by LAIGRET without obvious ill effects does not necessarily indicate that *rhesus* monkeys are more liable to develop encephalitis than human subjects. It is pointed out that LAIGRET's subjects were probably nearly all adults, whilst the *rhesus* monkeys used in laboratories are generally young animals and experiments have shown that the "haemato-cephalic barrier" is much more permeable in young animals than in adults. The authors consider that at present the simultaneous injection of neurotropic virus and immune serum is the best method to employ, as animal experiments show that it is much safer than the use of virus alone.

ix. The mouse protection test is considered of great value, but the question of its absolute specificity has not been proved conclusively. The importance of the viscerotomy test is emphasized and its use is advocated as a means of obtaining liver specimens in all countries where yellow fever might be suspected. With reference to vaccination, it is pointed out that no cases of yellow fever have occurred among any laboratory workers who have been vaccinated by either of the two methods in use, but it is necessary to follow the history of all vaccinated subjects in endemic areas. It is also emphasized that the use of vaccination does not authorize any relaxation in the continued application of general methods of control such as anti-mosquito measures, canalization of water, etc.

E. Hindle.

DESNOS (E. H.). Sur la fièvre jaune en Afrique occidentale. [**Yellow Fever in French West Africa.**]—*Rev. Méd. et Hyg. Trop.* 1935. May-June. Vol. 27. No. 3. pp. 127-149. [16 refs.]

A general account of the present position of yellow fever in French West Africa, based on statistical enquiries and also clinical observations by the author and his colleagues.

Tables are given showing the number of cases in French colonies each year from 1909 to 1933 inclusive. The author then gives particulars of other outbreaks previous to 1909 which were suggestive of yellow fever, followed by personal observations on atypical cases of the disease, both in natives and Europeans.

It is concluded that the disease shows oscillations in its distribution, importance and severity and among possible causes are suggested climatic variations; movements of masses of the population and works involving the use of much labour; the possible disappearance of immunity in the native; an insufficient knowledge of what animals may harbour the virus; and an incomplete knowledge of insect-carriers.

E. H.

ANNALES DE MÉDECINE ET DE PHARMACIE COLONIALES. 1935. Apr.-May-June. Vol. 33. No. 2. pp. 446-448.—Deux observations de fièvre jaune chez des indigènes de la région de Toumodi (Côte d'Ivoire). [**Two Cases of Yellow Fever in Natives from the Neighbourhood of Toumodi (Ivory Coast).**]

A record of two fatal cases of yellow fever in African negroes. The patients both showed typical clinical symptoms and also characteristic pathological and histological changes.

E. H.

ANNALES DE MÉDECINE ET DE PHARMACIE COLONIALES. 1935. Apr.-May-June. Vol. 33. No. 2. pp. 436-446.—Résultats des recherches concernant le test de protection contre la fièvre jaune dans les colonies françaises d'Afrique. [**The Results of Researches with Reference to the Protection Test against Yellow Fever in the French African Colonies.**]

A general account of the results obtained by various investigators in the study of the endemicity of yellow fever in French African colonies by means of the mouse protection test. The results have all been published previously, but the article in question furnishes a convenient summary. E. H.

SOPER (Fred L.). **Rural and Jungle Yellow Fever—a New Public Health Problem in Colombia.** (Lecture given before the Faculty of Medicine of Bogotá, April 5th, 1935.)—42 pp. With 13 figs on 6 plates. [31 refs.] 1935. Bogotá: Editorial Minerva, S.A.

A valuable summary of the subject, based mainly on the author's observations made under the auspices of the International Health Division of the Rockefeller Foundation and of the Departamento Nacional de Higiene of Colombia.

Most of the points discussed by the author have been dealt with by MORGAN [*ante*, p. 585] in his account of the Co-operative Yellow Fever Service in Brazil. After a description of recent laboratory and epidemiological progress in our knowledge of the infection, special attention is devoted to rural and jungle outbreaks. It is shown that suspected cases of yellow fever have been described from Muzo at various intervals since 1907, although the proof of its endemicity by protection tests was demonstrated only in 1931 and 1932, and proof of actual cases by autopsy only in March, June and October, 1934. Other outbreaks have also been identified at Caparrapi in 1933, and Restrepo in 1934. These cases occurred in the absence of *Aedes aegypti*, and some other species must be the carrier. The most common mosquito is *Haemagogus equinus*, the "blue" mosquito, which is a vicious biter in the field, generally attacking the feet and ankles, even when men are actively at work. This jungle yellow fever seems to be especially dangerous where the human population is least, but is in most intimate contact with jungle life and one is compelled to assume the existence of animal reservoirs of the infection. Monkeys abound in these neighbourhoods and out of five specimens collected at Muzo, four gave positive protection tests and the other inconclusive results.

There is little doubt as to the identity of the jungle yellow fever and the urban type since the clinical course and pathological changes are the same in both. Also cross-protection tests of known immune sera with the viruses from urban and jungle yellow fever are positive. In the laboratory yellow fever virus adapted to *Aedes aegypti* is readily transmitted by several other mosquitoes, and epidemics with and without *Aedes aegypti* have been observed in Bolivia as part of the same outbreak. Moreover, the most reasonable explanation of the Bucaramanga and Socorro epidemics is that the source of the epidemics was in nearby areas of jungle endemicity.

The difficulty of combating these jungle outbreaks is very considerable, and up to the present control measures applicable to such conditions are unknown. The protection of urban populations, on the other hand, is only a problem of administration and a list is given of the

recommendations of the Ninth Panamerican Sanitary Conference regarding yellow fever. Finally, the author outlines a program of studies in Colombia and urges the necessity of a yellow fever section of the National Laboratory.

The article should be read in its entirety by all those interested in the subject.

E. H.

LAIGRET (J.). La vaccination contre la fièvre jaune. [**Vaccination against Yellow Fever.**]*—Tunisie Méd.* 1935. June. Vol. 29. No. 6. pp. 225-234.

A general account of the subject with special reference to the method of vaccination advocated by the author and the results of its application in French West Africa.

E. H.

KOPCOWSKA (L.). Neuro-infection autostérilisée non mortelle avec présence d'inclusions intranucléaires, dans la fièvre jaune expérimentale du cobaye conférée par inoculation sous-durc-mérienne. [**Non-fatal Infection of the Nervous System with the Presence of Intranuclear Inclusions in Guinea-pigs Infected with Yellow Fever by Sub-dural Inoculation.**]*—C. R. Soc. Biol.* 1935. Vol. 119. No. 22. pp. 714-716.

The author has examined the brains of three guinea-pigs which were inoculated sub-durally with yellow fever virus and recovered without showing any definite clinical symptoms. Typical yellow fever inclusion bodies were found in all three animals, although many of these bodies were in course of disappearance. The inoculation of material from these guinea-pigs into normal guinea-pigs in no case resulted in the production of infection, showing that the virus had died out in spite of producing the typical intranuclear bodies.

E. H.

WHITMAN (Loring). **The Response to Yellow Fever Virus in the Non-susceptible Rabbit.***—Jl. Immunology.* 1935. Aug. Vol. 29. No. 2. pp. 99-110.

The authors tested the production of yellow fever antibodies in the rabbit, an animal which seems to be nonsusceptible to the infection.

Experiments with rabbits using neurotropic virus confirmed the view that there is no multiplication of virus in this animal after either intracerebral or intraperitoneal inoculation, since it fails to develop in the brain, and after 48 hours cannot be detected in the circulation.

The inoculation of virus, in every case, was followed by the development of antibodies capable of passively protecting susceptible animals against infection. The inoculation of a single dose of virus and subsequent protection tests in mice, showed that the titre of the serum depended to some extent on the amount of virus injected, the rabbits receiving larger doses giving higher titres than any of the others. Multiple injections were found to have little advantage over either single injections of an adequate amount, or two widely spaced injections. The most striking increase in titre was obtained by giving a second injection of virus into a previously immunized animal, after an interval of six or more weeks from the first injection, even small doses producing a serum titre ten to twenty times higher than that previously obtained. This increase is transient, but indicates the possibility of obtaining hyper-immune serum, and reducing the volume required for the present system of serum-virus vaccination.

E. H.

THEILER (Max) & WHITMAN (Loring). **Quantitative Studies of the Virus and Immune Serum used in Vaccination against Yellow Fever.**—*Amer. J. Trop. Med.* 1935. May. Vol. 15. No. 3. pp. 347-356.

An account of experiments in monkeys showing that the injection of living neurotropic virus, such as that used in human vaccination, is followed by a multiplication of the virus in the blood to a considerable concentration, unless previously a sufficient dose of immune serum is administered.

The results are of great importance in view of the two methods of yellow fever vaccination at present in use. They show, without any question, that if human beings are as susceptible to encephalitis as monkeys, the method advocated by SELLARDS and LAIGRET [see this *Bulletin*, Vol. 29, p. 572] is potentially dangerous to both the person vaccinated and the community.

This risk cannot be removed by reducing the amount of virus inoculated, for in monkeys infinitesimal doses seem, if anything, to be more likely to result in encephalitis than larger doses, even in the presence of small quantities of immune serum.

The inoculation of immune serum shortly before the administration of virus prevented the circulation of virus, and yet allowed active immunization. The amount of serum necessary is more closely related to the size of the host than the dose of virus, for even by reducing the virus component 100,000 times the dose of immune serum could only be reduced five times. Hyperimmune serum was found to be much more efficient, and smaller quantities were as effective as larger doses of average immune serum.

When the optimal amount of immune serum has been ascertained a wide range of virus concentration can be used with success, but minimal doses probably fail to produce immunity. E. H.

KOTTER (G. F.) & VAN DEN BERGHE (L.). Filtratieproeven van neurotroop gele koorts virus door Seitzfilters. [**Filtration Tests on the Passage of Neurotropic Yellow Fever Virus through Seitz Filters.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. June 30. Vol. 15. No. 2. pp. 213-220. With 1 fig. French summary.

The authors have tested the infectivity of Seitz filtrates of infected mouse brains. The results clearly indicate that the last part of the filtrate is more virulent than the first, the filter becoming more permeable to the virus after the passage of a certain amount of the suspension. It is recommended that when making tests of this nature it is advisable to use the last portion of the filtrate of the virus suspension. E. H.

NICOLLE (Charles) & LAIGRET (J.). La vaccination contre la fièvre jaune par le virus amaril vivant, desséché et enrobé. [**Vaccination against Yellow Fever by Means of Living Yellow Fever Virus Dried and "Coated."**]—*C. R. Acad. Sci.* 1935. July 29. Vol. 201. No. 5. pp. 312-314.

The authors mention that during the year 10,000 persons have been vaccinated against yellow fever by means of three injections of dried

virus [see this *Bulletin*, Vol. 31, p. 79]. Only three accidents have been recorded, two cases of meningitis and one of myelitis, but all the patients recovered.

With the object of reducing the number of inoculations the authors have tried the method of coating the dried virus with a layer of egg-yolk, or of olive oil, or with a double envelope of both agents. The object of this envelopment, or coating, which has been used by RAMON in the case of toxins, is to retard the diffusion of the material from the site of inoculation.

Twenty-two subjects have been inoculated with a single dose of either 320, 640, 800 or 4,000 mouse units of the dried virus, prepared in the usual way from infected mouse-brains but suspended in olive oil, neutralized and washed in alcohol. No local reactions were observed, and the rise in temperature on the 6th or 7th day, frequently seen after the ordinary vaccination, was always absent. Protective bodies appeared in the blood 19 days after the inoculation.

Another 21 subjects were vaccinated each with single doses ranging from 320 to 6,000 mouse units, similarly prepared, but suspended in egg-yolk (10 per cent. yolk in water). There were no local reactions or rises in temperature except in one case, where there was a slight fever on the 14th and 15th days. A series of 48 subjects were vaccinated each with 2,000 to 4,000 mouse units, similarly prepared but coated with two layers, one of egg-yolk and a second of olive oil. These inoculations produced no local reaction, no febrile attacks, nor any signs of anaphylaxis.

The authors advocate the use of single inoculations of the dried virus coated with egg-yolk as the simplest method of vaccination and consider that a dose of 320 mouse units is quite sufficient. E. H.

GRALL (Georges). Note sur le bakandjia ou fièvre rouge congolaise. [**A Note on "Bakandjia" or Red Fever of the Congo.**—*Ann. de Méd. et de Pharm. Colon.* 1935. Apr.-May-June. Vol. 33. No. 2. pp. 448-451.]

The description of the clinical symptoms observed in an epidemic of an eruptive fever during 1929 at Oubangui-Chari in the Congo.

The onset is characterized by general malaise, asthenia, stiffness in the back and limbs, and slight headache. After 24 to 48 hours there is an eruption of small red spots, at first generalized on the face, then spreading to the body and limbs, accompanied in most cases by moderate fever with slight bronchitis and diarrhoea. The eruption lasts 3 days, then disappears rapidly together with the accompanying symptoms, and the patient recovers completely in a few days without any sequelae. It attacks infants rather than adults and is benign, no fatal cases having been observed. The epidemic came from the north and travelled south from village to village along the main routes.

The disease is apparently well known to the natives of Banda and also to Europeans living in the Oubangui district. It is considered to resemble the disease described by CLAPIER in 1921 as a fever recalling dengue, and also that described by LEFROU at Brazzaville in 1928 and called by him "Fièvre rouge congolaise."

The author states that all the natives in this district who gave a positive yellow fever protection test had suffered from the above

mentioned disease when young, therefore he is of the opinion that the test is not specific unless one assumes a relationship between the two diseases, which is certainly not shown in the clinical manifestations.

E. H.

HOFFMANN (W. H.). La endemidad amarilla en el Africa.—Reprinted from *Sanidad y Beneficencia*. Habana. 1934. Vol. 37. No 7-12. pp. 346-357.

MATHIS (M.). Sur la nutrition sanguine et la fécondité de *Stegomyia*: *Aedes aegypti*.—*Bull. Soc. Path. Exot.* 1935. Mar. 13. Vol. 28. No. 3. pp. 231-234.

MORGAN (M. T.). Notes sur un voyage au Brésil pour étudier le service coopératif anti-amaril.—*Bull. Office Internat d'Hyg. Publique*. 1935. Aug. Vol. 27. No. 8. pp. 1504-1533. With 6 figs. (2 maps) [See this *Bulletin*, ante, p. 585.]

SOPER (Fred L.). El problema de la fiebre amarilla en América.—*Bol. Oficina Sanitaria Panamericana*. 1935. Mar. Publicación No. 98. 10 pp.

YAWS AND SYPHILIS.

TURNER (Thomas B.) & SAUNDERS (George M.). **Report of the Jamaica Yaws Commission for 1933.**—30 pp. With 7 maps & 12 charts. 1933. Dec. 31. Kingston, Jamaica, B.W.I.

In this, the second, report of the Jamaica Yaws Commission the problems under study during the year are dealt with in four main categories—(1) treatment, (2) transmission, (3) the relation of yaws and syphilis, (4) immunity. [For the first report see above, p. 50].

For all those interested in anti-yaws campaigns the methods adopted in Jamaica will have a particular interest. In the five areas surveyed 6,300, or 50 per cent. of all individuals, gave a history of yaws but of these only 652, or 5·2 per cent., presented lesions considered to be infectious although perhaps an equal number could be classed as potentially infectious; 96·2 per cent. of the infectious cases were treated. The effect of treatment was seen on re-survey, three months after a treatment campaign, of an area in which shifts of population were not marked, when only 17·5 per cent. of the number of infections originally observed were found.

As regards the evaluation of different drugs in treatment, it is stated that "the relapse rate for patients treated with bismuth salicylate is enormously higher than for those treated with neoarsphenamine." "Preliminary observations indicate that the beneficial results of treatment with the latter increase rapidly with the number of injections up to three and slowly thereafter." Halarsol and carbarsone were of little use; mapharsen may be found useful. The following table here reproduced shows results of treatment after one year:—

Drug	Clinical Diagnosis	No. of Cases	*Result Unsatisfactory		Serology after one year	
			No.	Per cent.	Wassermann. Per cent positive	Eagle Flocculation. Per cent positive
Neoarsph. ... 6 weekly doses ...	Infectious type	40	3	7·5	21·6	52·7
	Other ...	64	7	10·9	54·0	83·5
	Total ...	104	10	9·6	42·0	72·0
Bismuth salicylate 6 weekly doses ...	Infectious type	63	27	43·0	68·0	81·0
	Other ...	69	13	18·8	57·0	81·0
	Total ...	132	40	30·1	63·0	81·0

*Failed to heal or relapsed.

[Much work will have to be accomplished before the question of the treatment of yaws is established on a firm basis; the results above given cannot be considered as very satisfactory. Reference is made to working out "the time relation of infectious relapse to treatment"; when this is done it will probably be found that very much longer courses of treatment, probably combined treatment, will be necessary.]

Reference to the fly *Hippelates* was made in the first report. Further evidence is now adduced in support of the view that this insect plays an important part in the transmission of yaws in Jamaica. They feed with avidity upon open skin lesions in great numbers and *Sp. pertenuis* can be found later in the gut of the fly, actively motile up to 3-8 hours, while non-motile ones have been found in the oesophageal diverticulum or stomach in abundance after 48 hours. As many as 304 have been found in a single fly. Experiment shows that the spirochaetes were killed very rapidly by drying and that they lose their motility at once in contact with water or mud. Infectious material from yaws lesions on ringed slides kept at various temperatures was examined; at 37°C. marked decrease in motility of the spirochaetes in 1 hour, complete loss in 6 hours. At room temperature motility remained up to 8 hours. At ice-box temperature motility was preserved for 24-60 hours.

The conclusions come to in regard to yaws and syphilis upon a study of early cases of the two diseases as seen side by side in Jamaica are as follows:—Syphilis in the Jamaican negro resembles the disease in the negro in the United States. The cases of syphilis in rural Jamaicans resemble the disease as seen in the Jamaican negro town dwellers. Yaws in adults resembles yaws in children. Yaws in the town dweller differs in no way from yaws in the rural population. A comparative study of the disease picture in rabbits produced by 4 strains of *Sp. pertenuis* and 7 strains of *Sp. pallida* has shown significant differences which are regarded as characteristic of the two diseases.

The following note is of interest in regard to immunity. In 15 cases of yaws attempts to produce a lesion by homologous inoculation with virus failed, in one even before the generalized eruption had appeared. With heterologous virus inoculation, however, a lesion can be produced in a large proportion of cases.

The age of onset of yaws was determined in 6,353 cases. The peak of the curve is at about 7 years; 91 per cent. of all cases acquire yaws before the age of 15 years. The percentage of yaws males acquiring the disease after twenty is 1.7 as compared with 2.8 for females. The incidence of yaws varies in different districts from 40 to 60 per cent. Of 6,353 cases of yaws 1,694 or 26 per cent. showed lesions. Of these 10 per cent. were infectious and 16 per cent. non-infectious lesions.

About 56 per cent. of cases with lesions have had yaws less than five years, 80 per cent. of the infectious cases and 40 per cent. non-infectious. Among 518 cases there were 220 or 43 per cent. who had only ulcerative plantar yaws as their infectious lesion. Primary lesions occurred on the leg or foot—arm, hand, face—trunk in the proportion 91 : 15 : 6.

There appears to be no racial immunity. The following figures give the total number of each race and the percentages diagnosed as yaws cases:—Black 10,335-20.2; Brown 1,434-17.5; Chinese 712-10.1; East Indians 86-8.6; White 9-0. All the facts seem to point to chance of contagion and trauma as the two great factors in infection.

Some observations on neurological and cardio-vascular lesions were made. Cases exhibiting any type of paralysis were noted by the field survey inspectors. Thirteen cases out of a population of 12,500 were examined; of these 7 "showed lesions which are not uncommon in syphilis"; none gave a history of syphilis but all had had yaws—age 16, spastic paraplegia; 47 ? tabes; 25, hemiplegia; 45, paraplegia; 25, spastic paraplegia; 33, hemiplegia; 63, hemiplegia. The cardio-vascular cases were diagnosed at the clinic and consisted of 2 young

adult males with signs of aortitis and insufficiency. [The findings in these cases, however, go but very little way towards proving them to be framboesial in origin.]
H. S. Stannus.

JAMAICA. Report of the Jamaica Yaws Commission for 1934

[SAUNDERS (George M.), Clinical Director].—30 pp. With 7 graphs, 5 figs., 6 charts & 2 maps.

In this report for 1934, a brief account of the work done in the two previous years is given, followed by a description of the program carried through during the past year by the two treatment units, the Central Laboratory and the Special Unit. The results are presented in tabulated form and are unsuitable for summarization. The results of treatment with neoarsphenamine and bismuth salicylate are discussed. Both clinical findings and serological tests indicate that bismuth is the more useful drug when results are estimated without reference to existing climatic conditions.

A study of the relationship between rainfall and relapsing yaws lesions indicated that more lesions occur during the periods of high rainfall. Allowing for the effect of rainfall, the results obtained with neoarsphenamine would probably be slightly better than with bismuth. In areas subjected to control work for one year the number of persons with infectious yaws lesions at the end of the year was 14 per cent. of those at the beginning; the number of new infections in the year was 8 per cent. of the number for the previous year. Evidence is adduced to show that most infections are contracted by contact with other cases.

Further work on the "eye gnat"—*Hippelates pallipes*—as a possible vector of *Sp. pertenuis* is chronicled. "Transmission, probably by regurgitation of an infected 'vomit drop,' would occur only if flies fed on infectious lesions and then on non-infected ulcers or surface abrasions on the same day, with an interval of seven hours or less elapsing between the insects passing from the patient to the non-infected person." There was no evidence of any cyclical development of the spirochaetes in the flies. A fuller account of the entomological studies follows.
H. S. S.

KUMM (Henry W.). Annual Report—Entomological Studies made for the Jamaica Yaws Commission during 1934.—Report Jamaica Yaws Commission for 1934. pp. 19–30. With 5 figs. & 7 graphs.

Dr. Kumm brings forward evidence which very strongly suggests that the minute fly *Hippelates pallipes* is not only a potential but an actual carrier of the causative organism of yaws.

Dr. Kumm has observed *Hippelates pallipes* in enormous numbers on ulcers and has collected them at a rate equivalent to 5,000 flies per hour on one ulcer. The ulcers visited by flies are due to many causes of which yaws is the most frequent. It is observed that the flies will crawl under a scab and that they ingest large numbers of *Spirochaeta pertenuis*: moreover they feed intermittently, passing from man to man or man to animal. The *Sp. pertenuis* survives about seven hours in the anterior part of the gut of the fly and is probably transmitted by regurgitation.

The author's studies, which are very full, have shown that a number of Oscinidae closely related to *Hippelates pallipes* occur in Jamaica.

They may be easily trapped, but they are not attracted to man. It appears then that the one species alone is responsible for the transmission of yaws: this is supported by the rarity of the fly in Kingston, a place from which yaws is absent, though there are areas in Jamaica in which the fly is abundant in the absence of yaws.

A considerable section of the report deals with the bionomics of the flies, the time of day at which they feed, the meteorological conditions associated with their abundance and similar matters. The insect has been bred in the laboratory but the early stages have not been found in nature.

The report is an interesting piece of work based on a large body of fact. P. A. Buxton.

KUMM (Henry W.). **The Digestive Mechanism of One of the West Indian "Eye Gnats,"** *Hippelates pallipes* Loew.—*Ann. Trop. Med. & Parasit.* 1935. Oct. 5. Vol. 29. No. 3. pp. 283-302. With 3 figs. & 2 plates.

The author describes the anatomy and functions of the alimentary canal of *Hippelates pallipes*, an Oscinid fly concerned with the transmission of yaws in Jamaica.

The insect feeds on the surface of ulcers taking relatively great quantities of serum, and it has been observed that if it takes up *Sp. pertenuis* these organisms can live to about eight hours in the oesophageal diverticulum and for shorter periods in the mid-gut. During the first few hours after feeding it may frequently be observed that the fly regurgitates fluid on to the tip of the proboscis: sometimes the drop of liquid is swallowed again and it is suggested that the fly is passing it from the oesophageal diverticulum into the mid-gut in order to digest it. At other times the drop of fluid is deposited by the fly, and living *Sp. pertenuis* have been observed in it, so that presumably they might gain entrance to a second person by this mechanism. It is found that flies will deposit several spirochaetes per hour for the first few hours after feeding.

The mouth parts of this insect were described many years ago by GRAHAM-SMITH, who figured projecting spines on the pseudotracheae on the labellae. It appears that the spines are capable of cutting soft tissues and giving entry to micro-organisms. In the present paper the author extends our knowledge of the anatomy of the alimentary canal so far as it can be seen by dissection. P. A. Buxton.

KUMM (Henry W.), TURNER (Thomas B.) & PEAT (Alfred A.). **The Duration of Motility of the Spirochaetes of Yaws in a Small West Indian Fly—***Hippelates pallipes* Loew.—*Amer. J. Trop. Med.* 1935. Mar. Vol. 15. No. 2. pp. 209-223. With 3 figs.

Anyone who has watched flies feeding on yaws sores will have speculated upon the possible part they may play in the transmission of the disease, and some authors have laid stress upon the point. Thus SCHILLING (1770), cited by HERMAN, suggested that yaws was probably carried by a small fly, the "Yaws fly," in Surinam. NICHOLS in St. Lucia (1912) believed a fly which he called *Oscinis pallipes* to be the vector of the infection upon injured skin surfaces. WILSON and MATHIS (1930) thought that *Hippelates pallipes* acted in the same way in Haiti. Transmission experiments are, however, few. CASTELLANI

carried out some work with *Musca domestica*. More recently THOMSON and LAMBORN have published results obtained in Nyasaland.

The present paper deals with the fly *Hippelates pallipes*, the female of which is found to feed in enormous numbers on yaws lesions in Jamaica, estimated at 2,700 flies caught per man per hour.

Two hundred and sixty-nine flies were fed on yaws lesions containing spirochaetes in large numbers. In 78.1 per cent. *Sp. pertenuis* was found in the stomach or esophageal diverticulum or in both. In the 210 infected flies 3,617 *Sp. pertenuis* were counted. The majority of the organisms were found in the diverticulum during the first eight hours where they remain motile. Later they are found chiefly in the stomach where motility is rapidly lost. Very few spirochaetes remain in the proboscis, and those that do lose their motility quickly.

H. S. S.

TURNER (Thomas B.) ; SAUNDERS (George M.) ; JOHNSTON (H. M.), Jr.
Yaws in Jamaica. I. An Epidemiological Study of Two Rural Communities [TURNER & SAUNDERS].—*Amer. Jl. Hyg.* 1935. May. Vol. 21. No. 3. pp. 483-521. With 2 charts & 2 figs.
II. A Plan of Control based upon Treatment [TURNER, SAUNDERS & JOHNSTON, Jr.].—*Ibid.* pp. 522-539. With 1 fig.

In these two articles the authors deal with some observations collected in Jamaica during investigations made under the auspices of the International Health Division of the Rockefeller Foundation and the Government of Jamaica.

Two reports of the Jamaica Yaws Commission have already been published and received notice in this *Bulletin*. The present articles cover part of the same ground but deal in greater detail with the two sides of the subject mentioned in their titles. They are of great importance and should be read by all interested in anti-yaws work as it is the first time the problem has been tackled on anything like a proper basis.

It is not possible to condense the information contained in these papers but some idea of the subject matter may be drawn from the authors' own summaries :—

I.—“ 1. An epidemiological study of yaws was made in the communities of Bath and Seaforth in Jamaica, B.W.I. Pertinent data were secured on 94.8 per cent. of 2,708 inhabitants of the Bath area, and on 100 per cent. of 1,967 inhabitants in the Seaforth area.

“ 2. In the Bath area, 58.3 per cent. of the known population gave evidence of having had yaws, while in the Seaforth area the incidence of yaws among the total population was 47.3 per cent. In another, 6.8 per cent. and 5.9 per cent., respectively, blood Wassermann tests were positive in the absence of a history of yaws or syphilis. Only 0.5 per cent. of the population of each area presented evidences of having had syphilis.

“ 3. Among successive age groups of the general population of each area, there was a rise in the incidence of yaws up to the age of 15 years, after which a decline was noted. Among children aged 10 to 14 years the incidence was 75.2 per cent. for the Bath area and 59.3 per cent. for the Seaforth area. Yaws was many times more prevalent among children under the age of 5 years in the Bath area than in the Seaforth area.

" 4. Among more than 1,800 persons who had had yaws, in over 90 per cent. the disease was acquired before the age of 15 years.

" 5. The attack rate for the general population during each of two successive years was many times higher for persons under 20 years than for persons over this age. The attack rate among previously unaffected or non-immune persons was also much higher among children than among adults. In each area the highest rate was observed for the age group 5 to 14 years, although in general the rate for all age groups was higher in the Bath area than in the Seaforth area. The hypothetical level of infection for various age groups calculated from the observed attack rate among non-immunes was in close agreement with the actual level of infection found on survey.

" 6. In each area the incidence of yaws was higher among males than among females for nearly all age groups except children under 5 years of age. The difference was particularly marked among persons 5 to 20 years of age.

" 7. There were no consistent differences in the prevalence of yaws among children of different racial groups, although in the Bath area the incidence was lower among children of mixed white and negro blood than among pure negroes or East Indians.

" 8. In each area yaws was somewhat less prevalent among children belonging to the upper social-economic class than among those belonging to the lower class.

" 9. Yaws was less prevalent among children residing in the central village of each area than among those living in strictly rural areas. There is evidence which suggests that this was not due to differences in the standard of living of the two groups.

" 10. Over 90 per cent. of the cases of infectious yaws, in each area, were observed in persons under 20 years of age.

" 11. In approximately 75 per cent. of persons with yaws the initial lesion occurred on the lower legs or feet.

" 12. The bearing which these observations may have upon the problems of treatment and of transmission is discussed.

II.—" Methods are described which aim at the control of yaws by the reduction, through treatment, of the sources of infection in a community. The plan consists of three principal phases: first, a survey of all the inhabitants of a district to find those with infectious yaws lesions; secondly, treatment of these persons with appropriate drugs; and thirdly, subsequent supervision of the district by resurveys for the purpose of discovering new infectious cases which, in turn, are subjected to treatment.

" These measures are based upon the following observations: The clinical manifestations of yaws are such that persons with infectious lesions can be ferreted out from the general population with a high degree of efficiency by non-professional assistants (sanitary inspectors). In endemic yaws areas, over 90 per cent. of the patients presenting infectious lesions are under 20 years of age, and the total number of infectious cases is usually less than 10 per cent. of the general population.

" This plan of control has been applied in Jamaica to an increasing extent during the past 2 years. In one area, during the first year after treatment, the attack rate of yaws among susceptible persons was approximately one-fifth the rate for the 2 years preceding the institution of these measures. In other areas the results were equally promising.

"In a small series of cases the results of treatment with neoarsphenamine were found to be considerably superior to those with bismuth salicylate or halsarsol."

H. S. S.

PEÑA CHAVARRÍA (A.) & ROTTER (W.). **Frambesia in Costa Rica.**—*Puerto Rico Jl. of Public Health & Trop. Med.* 1934. Sept. Vol. 10. No. 1. pp. 129–132. With 8 figs. on 6 plates. [Spanish version pp. 125–128.]

A short note upon the occurrence of yaws in Costa Rica.

The disease has probably existed since the early days of colonization by Spain in Panama and Colombia and thence spread to Costa Rica. The disease probably exists in the interior of the country but appears only recently to have been introduced into the Atlantic section. Reference is made to the writings of FALLAS and VON BÜLOW (1925) and of NÚÑEZ (1925).

A couple of cases are described and figured and a note on the histology of a lesion is given: all are typical.

H. S. S.

BUTLER (C. S.). **Epidemiology of Yaws.**—*Arch. Dermat. & Syph.* 1935. Sept. Vol. 32. No. 3. pp. 446–450.

A short article in which an attempt is made to disprove four points made by HASSELMAN in 1931 in regard to yaws—" (1) limitation to the tropics, (2) spotty distribution, (3) lowered resistance of *T. pertenue* as compared with that of *T. pallidum*, (4) the effect of altitude in making the lesions of yaws centre in the mucocutaneous junctions."

The author believes that yaws occurs outside the tropics and in support of this belief cites the disease described as yaws in N. Carolina and Massachusetts by some authors of the middle of the 18th century and the treponematoses described by HUDSON in Syria and the disease described by GRIN in Yugoslavia. [Others reading the descriptions given by the several authors quoted have put another interpretation upon these observations.]

In regard to the spotty distribution of yaws and its limitation to non-urban native communities, the author says "It is absurd to contend that yaws stops at the outskirts of city communities where there is a world of eligible hosts inviting it to enter," and refers to a single observation in Guam to support his idea. [This in face of an enormous amount of evidence adduced by others.]

[Points (3) and (4) are hardly worth discussion as observations are too few to be of much value one way or the other.]

H. S. S.

BUTLER (C. S.). **On the Initial Lesion in Treponematoses Framboesiana.**—Reprinted from *Amer. Jl. Clin. Path.* 1935. May. Vol. 5. No. 3. pp. 231–237.

In this paper read before the Brooklyn Surgical Society the author reiterates some of his opinions concerning yaws, which may be summed up best perhaps in his own words—"I contend that yaws so-called is syphilis acquired usually by innocent contact." There is nothing essentially new and in great part the article is a criticism of experimental work on this disease.

H. S. S.

PELTIER (M.) & RIOU (M.). Présentation d'un malade. Syphilis ulcéro-végétante ou pian? [**Multiple Lesions: Framboesial or Syphilitic?**]*—Bull. Soc. Path. Exot.* 1935. Feb. 13. Vol. 28. No. 2. pp. 53-57.

The patient shown was a 29-year-old colonial infantryman with service in Morocco 1925-26, Indochina 1928-29, Morocco 1932-34, and a history of a spirochaete negative chancre on the penis in 1928. The chancre healed in three days after cauterization, the W.R. was negative, no treatment was given and he remained symptomless until the present illness developed in September 1934, the first lesion being a large vegetative one between the big and second toe. This was followed by a similar dark crusted lesion of the dorsal surface of the toe and then by an eruption on the trunk, accompanied by marked itching, some debility, a change in voice timbre and falling of the hair of the scalp and eyebrows.

When examined he presented large "papulo-végétante" plaques in two interdigital spaces of the left foot. On the body were seen some 30 "nummulaires" elements varying in size from a 50 centime piece to a 2 franc piece, brownish red in colour, not infiltrated. Others were noted on the scalp and forehead. Other lesions—"papules érosives et infiltrées," some covered with a brown crust, were discovered about the anus, the right labial commissure and in the left antecubital fossa. These lesions were definitely ulcerative. Treponemata were found in numbers in all the lesions. There was also redness and ulceration of the throat which cleared up without treatment. The authors faced with this rather unusual evolution suggest that the case may be one of yaws and not syphilis. [It seems to the reviewer that no good case has been made out for so regarding it.] H. S. S.

CARMAN (J. A.). **The Relationship of Yaws and Syphilis. Are they Two Diseases or One?***—East African Med. J.* 1935. Aug. Vol. 12. No. 5. pp. 135-149. [32 refs.]

An address given in Nairobi in which many of the well-known arguments for and against the identity of yaws and syphilis were discussed without perhaps adducing any new facts or new arguments. The author pronounces in favour of there being two separate diseases.

H. S. S.

SOLLINI (A.). Pian e sifilide unicismo o dualismo. [**Yaws and Syphilis: One or Two Diseases.**]*—Arch. Ital. Sci. Med. Colon.* 1935. Aug. 1. Vol. 16. No. 8. pp. 616-625. English summary (2 lines).

The author brings together the opinions of those who have written on the subject of the unity or duality of yaws and syphilis during the last 4-5 years and states them fairly. He then gives his own opinion, siding with the dualists. He maintains that many medical men join the service [he is speaking mostly of the Belgian Congo] when young and after ample training at home in the diagnosis of syphilis but with merely a theoretical knowledge of yaws; they naturally class doubtful lesions as syphilides, or take the word of an "infallible" sanitary officer. "In practice an elderly and conscientious colonial medical practitioner can distinguish at once and without any doubt a yaws

from a syphilitic lesion" (practica la quale permette ad un vecchio e coscienzioso medico coloniale di distinguere subito, senza incertezza un pianoma da un sifiloma). H. H. S.

HUDSON (Ellis H.). **Juxta-Articular Nodules in Euphrates Arabs.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Mar. 8. Vol. 28. No. 5. pp. 511–522. With 4 figs. on 2 plates. [42 refs.]

An interesting article reporting eight cases of J.A.N. among Arabs of the Middle Euphrates region and the pathological findings in one of these cases.

Of 236 unselected Bedouin males admitted consecutively to the clinic during 8 months, five or 2.1 per cent. manifested these lesions, recognized by the local name "*rik*." Of 8 cases described, six were male Bedouins, one a female Bedouin, one a townsman. All yielded positive W.R. and all gave a previous history of "*bejel*," the endemic native syphilis, from which 90 per cent. of the nomads and 40 per cent. of the townspeople suffer.

The author believes the lesions in his cases to differ in no way either clinically or pathologically from those described in cases of yaws and more rarely in cases of syphilis. H. S. S.

WOLF (Max). Zur Kenntnis der juxta-artikulären Knoten. [**A Case of J.A.N.**].—*Wien. Klin. Woch.* 1934. Nov. 23. Vol. 47. No. 47. pp. 1420–1422. With 2 figs. [15 refs.]

A report on a case of J.A.N. in a 34-year-old male syphilitic in Vienna.

The patient had lived in the province of Corrientes, South America during 1926–27, returning to Europe in May 1927. In August the same year he developed a spirochaete positive chancre and later the W.R. was positive. Courses of treatment with arsenic and bismuth were given during 1927 and 1928.

The J.A.N. lesions appeared in 1928, *i.e.*, while under treatment, on the index finger of the right hand and in the left hand in 1931. There were altogether nine nodules symmetrically situated on each hand and fingers and there was a syphilitic bursitis over the olecranon. The nodules were partly attached to the deep surface of the skin but moveable over the deeper tissues. They gave to the skin stretched over them a yellowish colour. There was no interference with joint movements. The largest was the size of a cherry; in some there was a suggestion of softening but in none did the skin break down. In 1931 the patient sought relief; 5 injections of salvarsan and 8 of bismuth were followed by retrogression of the nodes.

The author suggests that the special localization was due to the man constantly driving a motor car. The histological picture he thinks suggests a syphilitic lesion but spirochaetes were not demonstrated.

H. S. S.

HACKETT (C. J.). **Interstitial Keratitis, Boomerang Legs and Yaws in a European Boy from the New Hebrides.**—*Med. Jl. Australia.* 1935. Aug. 17. 22nd Year. Vol. 2. No. 7. pp. 213–216. [21 refs.]

A boy aged 14 was brought for treatment in Australia suffering from blepharospasm, swelling of the lid and ciliary congestion of right eye in

1933. The cornea was hazy, the iris swollen and vascularized and a small hypopyon was present. This was followed after a few weeks by affection of the left eye. The condition was considered to be one of interstitial keratitis. Further clinical examination revealed bilateral "boomerang tibia" it was believed of 5 years' duration and a little subcutaneous nodule on one wrist followed by the appearance of a nodule on the other wrist.

"Both tibiae showed swelling anteriorly (with the maximum point just above the middle of each bone) which gave the impression of forward bowing. There was slight lateral swelling. The anterior tibial crest was rounded." There was an increase in the antero-posterior diameter in the middle third. This was confirmed by radiological examination and the report stated that the condition was "suggestive of specific periostitis." Under treatment with N.A.B., etc., the eye condition subsided and the nodules disappeared. The blood W.R. was positive; the C.S.F. was normal.

The author suggests that it is only reasonable to suppose that the interstitial keratitis and the sabre tibiae were due to the same cause—either congenital syphilis or yaws, and believes that the latter is the more likely.

The boy had lived in the New Hebrides, where yaws is common and syphilis said to be absent, from birth to the age of $2\frac{1}{2}$ years and again from the age of $5-7\frac{1}{2}$ years. The rest of his life including the last 6 years was passed in Australia. But beyond having had some sores about the ankles as a child, sores which occur in all the children, and an abscess of uncertain nature in the right thigh in 1928 before the appearance of the tibial condition, there was no history of yaws.

Against the condition being due to congenital syphilis was the fact that the father and two brothers gave negative W.R. and the history of the mother's 6 previous pregnancies. It is also pointed out that interstitial keratitis has been previously by other writers ascribed to yaws.

H. S. S.

MONTESTRUC (E.). Un cas de goundou à la Martinique. [**A Case of Goundou in Martinique.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 770-771.

A case of goundou in a 23-year-old Martinique male seen at Fort-de-France.

Beginning 2 months before, on examination there were symmetrical paranasal bony hard tumours the size of small hazel nuts. No other signs nor symptoms, no bony deformities elsewhere; no history of yaws or syphilis (Vernes péréthynol: 0); no history of nasal discharge.

This is the first case to be reported from the French Antilles though BRANCH reported a case from St. Vincent, an adjoining island. In both, yaws and syphilis are endemic. The author believes it is a disease independent of yaws.

H. S. S.

WALKER (J.) & MATHIEU (V.). Contribution à la question du pian et des rhumatismes pianiques en particulier dans le Ruanda-Urundi. [**Yaws and Rheumatism in Ruanda-Urundi.**]—*Ann. Soc. Belge de Méd. Trop.* 1935. Mar. 31. Vol. 15, No. 1. pp. 119-125.

An attempt to correlate the rheumatism so common among the natives of Ruanda-Urundi, as elsewhere in Africa, with latent yaws.

The authors believe that syphilis, and therefore congenital syphilis, is rare among this native population, basing their belief upon the fact that among 7,000 persons examined in 1933, in only 22 was there a penile lesion of possibly syphilitic nature, and that of these in only 16 was the *Sp. pallida* demonstrated. [Reasoning open to fallacy.]

They therefore assume that positive serum reactions are due to yaws in the vast proportion of cases and that syphilis may be neglected.

In attempting to find the percentage of the population with latent yaws, Wassermann and Meinicke reactions were carried out upon 174 adult persons who had no history of yaws, who had no sign of yaws and who had no other disease likely to influence the reactions.

In 119 or 68.4 per cent. both reactions were negative and these cases were considered to be clearly "indemnes de pian." Twenty other cases or 11.5 per cent., in which the reactions were doubtful were considered non-framboesial.

The remaining 35 or 21 per cent. were believed to be cases which should be looked upon as cases of latent yaws. In regard to rheumatism or "douleurs rhumatoides" 446 adults were selected, complaining of this symptom but exhibiting no signs of yaws, and their serum reactions carried out. In 47.1 per cent. the reactions were completely negative, in 34.1 per cent. positive and in others partly positive so that it was considered that half the cases of rheumatism were of framboesial origin. [A suggestion that may be true but is not proved as the authors seem to agree later.]

To account for the high figure of 21 per cent. latent infections, *i.e.*, persons with no history, sign or symptom of yaws the authors believe they have good grounds for suggesting that the number of infections in childhood which are benign and undergo spontaneous cure leaving no trace behind them, except the positive serum reaction, is much greater than is generally believed. H. S. S.

HASSELMANN (C. M.). **Fatality from Exacerbation of Latent Tuberculosis due to Thio-Bismol in a Case of Yaws.**—*Arch. Dermat. & Syph.* 1935. May. Vol. 31. No. 5. pp. 686-691. With 1 fig. [17 refs.]

A case of yaws in which death followed upon the injection of bismuth.

A child aged 9 years suffering from florid yaws but otherwise apparently in good health was given 3 intramuscular injections, 3 days intervening between the treatments. The first injection consisted of bismuth hydroxide dispersed in oil, the second of a 10 per cent. suspension of bismuth salicylate in oil, these two together being equivalent to 0.248 gm. bismuth. The third injection consisted of 0.2 gm. thio-bismol containing 0.075 gm. bismuth. Two days later fever and scanty urine were noted and death occurred on the 6th day after the last injection. Post-mortem examination revealed a fatty congested liver, tubular nephrosis and fibrocaseous pulmonary tuberculosis.

The author points to the danger which is likely to follow upon the fashion to overemphasize the efficacy and harmlessness of the various bismuth preparations in the treatment of yaws and syphilis. He holds that there is "no direct need for combining arsphenamine with bismuth" and believes, with LESSER, HUDELO and RABUT, STOKES and others, that the action of bismuth is one of inhibition and not destruction of the treponeme. "It is high time and quite necessary to draw attention to the mostly transient and rather inconstant effects on the

malady on the one hand and the increasing number of toxic side-effects on the other." Bismuth is far inferior to arsphenamine but if it is used then oily preparations are to be preferred to water soluble compounds. Attention is drawn to the particular liability of bismuth to awaken and cause exacerbation of tuberculous lesions.

H. S. S.

COUTINHO (Arthur). Um novo medicamento no tratamento da boubá. [A New Drug for Treatment of Yaws.]—*Ann. Paulist. Med. e Cirurg.* 1934. Dec. Vol. 28. No. 6. pp. 555-559. With 2 figs.

Vanadium like bismuth and arsenic has been used in the treatment of syphilis but its toxicity was greater than that of the two latter. Recently Professor PEREIRA has introduced a newer compound called Tarvan, sodium vanadium tartrate, in the treatment of syphilis, which combines a marked spirochaeticidal action with diminished toxicity.

This preparation has now been tried out in Brazil by the author on two cases of florid yaws. Six intramuscular injections in one case, three in the other, at 3-4 days intervals, the dose being 2 cc. of a 7.5 per cent. solution, caused complete disappearance of the yaws eruption and cessation of bone pains and headache, the only unpleasant symptom being nausea following the earlier doses.

The author states that the cost is low and is persuaded that it is a most efficacious remedy. Spirochaetes disappeared from lesions in 48 hours after the first injection. [The "blanchissement" obtained in these two cases would appear to be insufficient grounds upon which to base an opinion of much value. No mention is made of Wassermann reaction.]

H. S. S.

WILSON (Paul W.). Incidence of Yaws and Syphilis in Five Rural Villages, Republic of Panama.—*U.S. Nav. Med. Bull.* 1934. Oct. Vol. 32. No. 4. pp. 391-401.

A report upon the study of the incidence of yaws and syphilis in villages near Panama City.

A large part of the paper is taken up with serological reactions presented in the form of tables which cannot be summarized, the rest deals with individual cases which need not be reproduced.

J.A.N. were found in 10 per cent. of the yaws cases and it is called to mind that in Haiti the figure was only 0.42.

H. S. S.

LAFLEUR. Contribution à l'étude des croyances des indigènes de la haute Sangha au sujet du pian.—*Ann. de Méd. et de Pharm. Colon.* 1934. Oct.-Nov.-Dec. Vol. 32. No. 4. pp. 574-579.

MEMORSKIJ (W.). Nodositas juxtaarticularis ohne Syphilis.—*Arch. Dermat. u. Syph.* 1935. Aug. 14. Vol. 171. No. 6. pp. 610-611.

NÄGELSACH (E.). Myorezidiv bei Frambösie.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1935. Mar. Vol. 39. No. 3. pp. 125-126.

TROPICAL OPHTHALMOLOGY.

A REVIEW OF RECENT ARTICLES. XXIV.*

Conjunctiva.—Saradindu SANYAL¹ has isolated Gram positive cocci in plasma cells obtained from cases of the epidemic conjunctivitis and keratitis met with in Calcutta during recent years. These cocci are also found in the epithelial cells and may be seen lying free in the sub-epithelial connective tissues.

Trachoma.—Slight ptosis which gives the patient a sleepy appearance is a constant early sign in the first stage of trachoma. BUSACCA² attributes this to the increased weight of the lid caused by the oedema associated with the inflammation in the upper fornix and disagrees with FALTA's theory that it may be due to an involvement of the tarsal muscle in the inflammation.

WRIGHT³ has contributed an important paper regarding the disease in which he states that, working in conjunction with Dr. C. G. PUNDIR and the staff of the King Institute, a virus has been isolated on the allantoid membrane of the chick from cases of undoubted trachoma. The virus is filtrable and the filtrates reproduce similar lesions on the allantoid membrane. Hitherto, however, attempts to reproduce the disease in the human subject by implantation of the virus have been unsuccessful. The author deplures the obstacle to research presented by the difficulty clinicians experience in deciding what constitutes true trachoma. He believes that it is a specific disease entity and that the development of cicatricial tissue is one of its outstanding features; this is, however, an extremely variable feature and cannot alone be used by experimentalists as a criterion of trachoma. The extraordinarily heavy incidence of the disease amongst the Sikh and other regiments stationed in the Punjab and North-West Provinces described in the report of the Public Health Commissioner with the Government of India is referred to with some scepticism, and the value of Wilson's sign is contested. The whole problem of the disease is compared to that of dysentery which at one time was regarded as a single disease entity and is now differentiated into a number of varieties. A much needed warning is given against the too strenuous treatment by caustics of conjunctival disorders which would be likely to recover if subjected to a mild and harmless drug treatment with lavage. MEIGHAN⁴ has described the measures taken in Glasgow where the disease is a notifiable one. At the end of 1934 there were 120 cases on the register, but 13 of these were doubtful. During the year there were 17 notifications and 7 of these had definite trachoma. There is a central dispensary where a surgeon diagnoses and treats the cases whilst a nurse visits the homes and keeps contacts under observation and carries out treatment.

* For the twenty-third of this series see Vol. 32, pp. 471-478.

¹ SANYAL (Saradindu). A Preliminary Report on the Bacteriology of Kerato Conjunctivitis with Adenitis seen in Calcutta.—*Calcutta Med. Jl.* 1935. May. Vol. 29. No. 11. pp. 621-622. With 1 plate.

² BUSACCA (Archimède). A propos d'une remarque de M. Falta sur mon article "Ptosi transitorie e ptosi permanenti nel tracoma."—*Rev. Internat. du Trachome.* 1935. July. Vol. 12. No. 3. pp. 166-168.

³ WRIGHT (R. E.). The Trachoma Problem.—*Brit. Jl. Ophthalm.* 1935. June. Vol. 19. No. 6. pp. 309-318.

⁴ MEIGHAN (S. Spence). Trachoma in Glasgow.—*Brit. Jl. Ophthalm.* 1935. June. Vol. 19. No. 6. p. 326.

Fifty-nine per cent. of the patients were under fifteen years old. ROQUES⁵ advocates the application of formol in the treatment of the disease. The drug is applied to the everted lid after thorough cocaineization and drying of the membrane. A moistened swab is kept in contact with the conjunctiva for a minute and this is followed by an abundant irrigation with distilled water. A five per cent. solution appears to have given the best result. MACCALLAN⁶ has discussed some aspects of trachoma. He defines the disease as "a specific contagious disease of the conjunctiva characterized by the new formation of lymphoid tissue which spreads to the cornea. It is followed by cicatricial changes in the affected tissues. It is chronic in nature." The aetiology is uncertain and the presence or absence of inclusion bodies is not of diagnostic significance. He believes that the experimental conjunctivitis produced in monkeys by the inoculation of trachomatous tissue is true trachoma despite the fact that the cornea remains free from invasion. No reference is made to Noguchi's *Bact. granulosis*. The epidemics of acute conjunctivitis which occur in trachomatous countries and are responsible for the high incidence of blindness therein add to the aetiological difficulties. These ophthalmias complicating trachoma are responsible for the heavy incidence of blindness in some countries. In the great majority of countries where trachoma is endemic, however, the disease begins insidiously and pursues a chronic course. Infection in childhood is mostly familial, but may result from a mass infection in a boarding school. The issue of simple eyedrops by the Government for use as a prophylactic in badly affected countries might be of service. It is stated that in some parts of Northern India trachoma is practically universal, but progresses to a quiescent stage which produces little disability. [This seems to be an exaggerated estimate if the author's definition of the disease is accepted.] HERBERT⁷ has commented on BUSACCA's description of the microscopical features of "Herbert's Pits" (*ante*, p. 472). He suggests that the epithelial crypts found at the limbus in some eyes induce a lymph stasis in their neighbourhood which favours the accumulation of wandering cells. In trachomatous infection erosion of the corneal lamellae occurs and pitting results. In his Indian experience there was but little indication of any epithelial proliferation in the pits; possibly this was due to lack of treatment and absence of any epithelial stimulant. The experience in Lithuania of AVIZONIS⁸ is distinctly unfavourable to the theory that trachoma and pterygium are mutually antagonistic. He has, indeed, found that trachoma may, if anything, render a person more susceptible to the growth.

CULLOM⁹ has described some of his trachoma experiences. These show that trachoma is a transmissible disease carried by infectious secretion from one eye to another. He thinks, too, that this secretion

⁵ ROQUES (Henry). Nouveau traitement chimique du trachome.—*Gaz. hebdomadaire de Médecine de Bordeaux*. 1935. Mar. 31. Vol. 56. No. 13. pp. 198-200.

⁶ MACCALLAN (A. F.). Trachoma—Recent Advances and the Principles of Prophylaxis.—*Brit. J. Ophthalmol.* 1935. May. Vol. 19. No. 5. pp. 253-260.

⁷ HERBERT (H.). Corneal Pitting.—*Brit. J. Ophthalmol.* 1935. May. Vol. 19. No. 5. pp. 261-264.

⁸ AVIZONIS (P.). Le pterygion et le trachome.—*Rev. Internat. du Trachome*. 1935. Apr. Vol. 12. No. 2. pp. 97-98.

⁹ CULLOM (M. M.). Trachoma Infection and Treatment.—*Southern Med. J.* 1935. July. Vol. 28. No. 7. pp. 642-645.

may cause a very violent reaction. If the infection is feeble and ordinary cleanliness is observed, chances of contagion are slight. The disease is a filth disease due to the indiscriminate common use of towels and wash-basins. He is rather sceptical of the statement that pannus occurs independently of the rough surface of the lid and thinks the obvious explanation is that it is a traumatic injury to the cornea which causes abrasion and ulceration of the epithelial layer. He stresses the importance of attending to any malnutrition which may be present.

As the result of laboratory work at Giza, STEWART¹⁰ has put forward the hypothesis that the granular virus of trachoma is introduced into the conjunctiva in the bodies of bacteria of several species. These bacteria, acting as intermediate hosts, are phagocytosed to form the Prowazek-Halberstaedter bodies. The granules of the virus are liberated by the bursting of the inclusions and are then dispersed through the conjunctiva. Prowazek-Halberstaedter bodies are not found in pure, uncomplicated trachoma, but only in trachoma complicated by bacterial infection, especially the Koch-Weeks bacillus and the gonococcus.

VON SZILY¹¹ found that he was able to induce a follicle formation in the uvea and other ocular and orbital tissues by inoculating material obtained from a case of sympathetic ophthalmitis. This led him to experiment with trachomatous matter in a similar fashion. The matter was ground in a mortar with saline and the emulsion injected into the vitreous of a rabbit after having punctured the anterior chamber. Many of the experiments were negative; but in some he was successful in inducing a typical follicle formation. He suggests that some ultra-microscopic organisms may exist which have the property of bringing about follicle formation. SÉDAN¹² has reported three cases which he believes to have been trachomatous and in which a relapse of the conjunctival inflammation occurred during an attack of hay-fever, bronchitis and influenza in the respective patients. PADOVANI¹³ expresses himself satisfied with the use of taurocholate of soda in the treatment of pannus and quotes two of his cases as evidence. The fact that the drug is capable of inducing lysis of certain bacteria *in vitro* suggested its employment. He used a solution of 10 per cent. to paint the anaesthetized conjunctiva; but he recommends a weaker solution of 3 per cent. as an instillation if corneal ulceration is present.

JOURDRAN¹⁴ has reported from Tonkin seven cases of trachoma which he claims to have cured completely within a remarkably short period by the use of high frequency fulguration. The operation is only slightly painful; it induces a rather marked oedema which gradually disappears.

¹⁰ STEWART (F. H.). Recent Advances in Trachoma.—*Brit. Med. J.* 1935. June 22. pp. 1261-1262. [15 refs.]

¹¹ VON SZILY (A.). Uebertragungsversuche mit Trachommateriel. Ein Weiterer Beitrag zur Kenntnis follikelbildender Erreger.—*Klin. Monat. f. Augenheilkunde*. 1935. Jan. Vol. 94. pp. 1-11. With 21 figs.

¹² SÉDAN (Jean). Trois cas de trachome "saisonnier."—*Rev. Internat. du Trachome*. 1935. Apr. Vol. 12. No. 2. pp. 91-94.

¹³ PADOVANI (S.). De l'action favorable du taurocholate de soude dans le trachome. (A propos de l'hypothèse du rôle étiologique des inclusions.)—*Rev. Internat. du Trachome*. 1935. Apr. Vol. 12. No. 2. pp. 94-97.

¹⁴ JOURDRAN. Contribution à la thérapeutique du trachome par l'étincelle froide de haute fréquence (courants de tension, fulguration monopolaire).—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934*. Vol. 2. pp. 523-527.

Cornea.—WRIGHT¹⁵ has reported two cases of *corneal grafting* which show that large corneal grafts are just as likely to be successful as small ones and that an eye blind from glaucoma constitutes a good donor eye. Anterior synechiae can be dealt with successfully and the chamber reformed by performing a preliminary operation. One of the patients had trachoma with pannus and a corneal ulcer and the other had suffered from a syphilitic interstitial keratitis. The larger graft was 9 mm. in diameter.

Cataract.—HOUWER & MINGELEN¹⁶ believe that in the tropics infra-red rays play an important part in the aetiology of senile cataract. Other factors, too, are of course present. Heredity, endocrine disorders, autointoxication and senility are instances. They base their conclusions on the fact that they have found a high incidence of "furnace workers' cataract" in Java amongst people who have never been exposed to a furnace glare. The proportion of Europeans affected by glassblowers' cataract was greater than that of the natives of Java.

Glaucoma.—ELLIOT¹⁷ has reviewed some of his experiences in connexion with his operation for glaucoma. He warns the surgeon against dragging uveal tissue into the trephine hole; this can be avoided if the trephined disc and the bulging iris are seized with one grip of the forceps and cut together with one snip of the scissors. He advocates a small peripheral iridectomy and uses a continuous suture to unite the edges of the conjunctival flap, passing the thread over iodine before and after each penetration of the conjunctival edges. Impaction of uveal tissue which blocks the trephine hole and stops filtration may prove difficult to deal with. Recently he has been successful in treating such a case by passing a Ziegler's knife subconjunctivally and dividing the tissue with a sweep of the knife. Detachment of the choroid may occasionally occur after trephining. It is unnecessary to keep patients with this complication in the recumbent position. The main point in post-operative treatment is to ensure that the pupil remains wide. Massage after trephining is of great value. Should it prove necessary to remove the lens for cataract after trephining has been performed, care should be taken to avoid involving the trephine aperture in the incision and to make the conjunctival flap in an area free from filtration.

Mycosis.—LANGERON¹⁸ has reported a case of ocular mycosis. One eye only was affected. In the upper quadrant of the cornea and involving the neighbouring conjunctiva lay a pea-sized nodule surrounded by an area of infiltration. The surface showed three small yellowish pustules, the largest of which lay on the corneal aspect and was breaking down. A yellowish ulcer the size of a lentil was seen on the upper tarsal conjunctiva, whilst small rounded greyish-yellow raised spots covered the upper cul-de-sac. The changes were limited to the upper lid. The glands were swollen, but freely moveable and not painful. Febrile reaction was absent. A fungus of the *Beauveria* type was isolated from the lesion; the author has named it *B. brumpti*.

¹⁵ WRIGHT (R. E.). Corneal Grafting. Reparative and Optical.—*Brit. J. Ophthalm.* 1935. June. Vol. 19. No. 6. pp. 341-347. With 1 fig.

¹⁶ HOUWER (A. W. Mulock) & MINGELEN (R.). Cataracta Tropica.—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 509-513.

¹⁷ ELLIOT (R. H.). Some Points in Connexion with Sclerocorneal Trephining.—*Brit. Med. J.* 1935. Aug. 24. pp. 334-335.

¹⁸ LANGERON (Maurice). Mycose oculaire primitive due au "*Beauveria brumpti*."—*Bull. Acad. Méd.* 1934. Jan. 23. 98th Year. 3rd Ser. Vol. 111. No. 3. pp. 133-137.

Onchocerciasis.—JOYEUX, SÉDAN & ESMENARD¹⁹ have reported a case of ocular onchocerciasis in a European who had been on the Ivory Coast in French Western Africa for a little over a year. The patient had a subcutaneous nodule over his left shoulder-blade from which it was possible to obtain a dead *O. volvulus*. There were numerous small granulomata under the conjunctiva, but no microfilariae were found in these.

COHEN²⁰ has described a sign which is present in the early stage of a paralysis of the facial nerve. If the normal person is asked to look upwards whilst keeping the eyes closed the action of the *levator palpebrae superioris* is masked by the contraction of the *orbicularis*; but if there be any weakness of the latter muscle the eye opens on looking upwards owing to the feeble action of the *orbicularis*. (This may prove a valuable sign in the early stages of leprosy.)

Retinitis pigmentosa.—Many forms of treatment have from time to time been employed in attempts to alleviate this condition. MACDONALD & MCKENZIE²¹ have been unable whole-heartedly to confirm ROYLE's successful results by the performance of a sympathectomy. Their experience was limited to four cases; one of these regressed, one remained unaltered, and the other two showed a slight improvement. The authors suggest that to have a fair chance the operation should be performed in the very early stages of the disease.

Quinine amblyopia.—WOLFF²² investigating the causes of *quinine amblyopia*, points out that quinine interferes with the oxidation of the tissues. This oxygen lack causes a spasm of the retinal artery and leads to the changes associated with quinine poisoning. He thinks that two stages may be distinguished in the action of the drug. In the first the quinine in its capacity as a general protoplasmic poison acts directly on the retinal elements, and the second stage depends on the spasm of the retinal vessels and is probably acute in onset.

The Twenty-first Annual Report of the Ophthalmic Section of the Government of Egypt for the year 1933 records the continuous progress made in the fight against diseases of the eye in that country. The statistics deal with the diseases seen in the enormous number of 825,304 new patients, an increase of 15 per cent. compared with the previous year. 6.4 per cent. of the total were found to be blind in one or in both eyes and 80 per cent. of this blindness was caused by acute ophthalmia. Nearly half the acute ophthalmias were due to the gonococcus. 10,066 primary school-children were examined and it is stated that the appalling proportion of 98 per cent. was affected by trachoma in some form. 59,670 cases of trichiasis were seen amongst the new out-patients, and 8,533 cases of chronic dacryocystitis. Trachoma accounted for 761,289 admissions. Cases of primary chronic glaucoma (6,223) considerably out-number those of senile cataract (4,655); this incidence differs from that found in most tropical countries and the cause of it is worthy of investigation.

H. Kirkpatrick.

¹⁹ JOYEUX (Ch.), SÉDAN (J.) & ESMENARD (J.). Un cas d'onchocercose contractée à la Côte d'Ivoire, avec complications oculaires.—*Bull. Soc. Path. Exot.* 1935. June 12. Vol. 28. No. 6. pp. 435-438.

²⁰ COHEN (Henry). An Early Ocular Sign in Facial Paresis.—*Brit. Jl. Ophthalm.* 1935. May. Vol. 19. No. 5. p. 267.

²¹ MACDONALD (Alexander E.) & MCKENZIE (Kenneth G.). Sympathectomy for Retinitis Pigmentosa.—*Arch. Ophthalm.* 1935. Mar. Vol. 14. No. 3. pp. 362-373. With 6 figs.

²² WOLFF (Eugene). The Causation of Quinine Blindness.—*Lancet.* 1935. June 29. pp. 1497-1498. [14 refs.]

MISCELLANEOUS.

EGYPT, MINISTRY OF THE INTERIOR. DEPARTMENT OF PUBLIC HEALTH. **The Research Institute and the Endemic Diseases Hospital. Third Annual Report 1933.**—108 pp. With sketch maps, 3 graphs & 7 figs. on 4 plates. 1934. Cairo: Government Press, Bulâq.

This report, which is published over the signature of the Director (Dr. M. KHALIL), details the work carried out by the staff of the Institute and the Hospital, which includes a biochemist, a protozoologist, an entomologist, a malarial officer and four physicians.

The report is divided into Scientific and Clinical Sections, the former dealing with the work of the specialists and the latter detailing much interesting work on the anaemias, schistosomiasis, hepato-splenomegaly, malaria, ancylostomiasis, pellagra and dysentery. Attention is called to the rarity of pernicious anaemia in Egyptians, though parasitic anaemias are common; of over a hundred cases of achlorhydric anaemia not one was found to be macrocytic in type.

The observers express dissatisfaction with the accuracy of the haemocritometer which in their hands gave 20 per cent. of errors and has been given up in favour of the Price-Jones curve and measurement of the volume index. A few observations were made on Archibald's claim regarding the lethal effects of *Balanitis aegyptiaca* on disease-carrying molluscs. Their results show that *Planorbis* and *Bulinus* are killed by a 1 in 10,000 solution of the berries in 48 hours, but the experiment deserves to be repeated on a scale more worthy of its importance. The tree is not, however, indigenous to northern Egypt.

Oriental sore is shown to be common in certain villages and a survey of five of these with a total population of 1,400 revealed no less than 232 persons with active sores and 341 healed ones.

Phlebotomus papatasi is the common sand-fly.

The part devoted to malaria is full and interesting but is too long to be summarized here.

An analysis of the infections amongst patients attending the helminthological clinic shows that about half (6,877 out of 12,804) suffered from urinary schistosomiasis whilst only about 2 per cent. harboured the intestinal worm (*S. mansoni*).

Fouadin was used for treatment and of those who received the full course of nine injections 83 per cent. were cured and on the re-examination of 480 patients a month later 87 per cent were still negative.

Ancylostomiasis was the second most common worm infection and was treated by 5 cc. doses of carbon tetrachloride with results which varied according to the number of treatments given; 58 per cent cured after one treatment, 73 after two, 93 after three and all after four treatments.

The Clinical Section deals with investigations on in-patients who offer better opportunity for thorough and exact observation.

The study of helminthic anaemias is of particular interest; it is noted that severe grades are produced by ancylostomes and intestinal schistosomes, moderate grades by urinary schistosomes and by ascarids whilst the other helminths do not produce any anaemia (*T. saginata* is the only tape-worm referred to).

The degree of eosinophilia bears no relation to the intensity of the worm infection but is dependent on the condition of the host, and in the

same way the severity of the anaemia bears no direct ratio to the number of the worms, but here again it is the human reaction which is the determining factor. A rise in the eosinophile count is indicative of a good response to treatment just as is a rise in the reticulocyte count.

The observers emphasize that the type of anaemia common to helminthic infection is "hypochromic, micro- or normocytic, non-haemolytic, hypoplastic anaemia with eosinophilia."

Such cases derive no benefit from massive liver treatment but respond to large doses of iron.

The disease hepato-splenomegaly is of particular interest and there is much in the report concerning its nature. These observations were made on 103 cases, of which 67 were associated with intestinal schistosomes and 23 with the urinary infection. They emphasize the fact that a number of other conditions must be excluded (*e.g.*, syphilis, malaria, leishmaniasis, Hodgkin's disease, Gaucher's disease, etc.) before a diagnosis of Egyptian splenomegaly can be arrived at. The bilharzia cutaneous reaction has been used and the observers regard a negative reaction as strong evidence against infection, whereas, in a highly infected country like Egypt, a positive reaction is of less value in that it does not distinguish between a recent and a past infection.

It is satisfactory to feel that such good use is being made of the unrivalled clinical material in Northern Egypt and we look forward to further reports and hope that they will include summaries of those researches which in the present publication are incomplete.

F. P. Mackie.

CAVALADE. Rapport sur une tournée effectuée dans la région de Niamey (Niger) par le groupe mobile d'hygiène en juin-juillet 1933. [*Account of a Tour in Niamey (Niger) District.*]*—Ann. de Méd. et de Pharm. Colon.* 1935. Apr.-May-June. Vol. 33. No. 2. pp. 363-384. With 1 map.

This is a report of a tour of inspection carried out from Niamey to Kouré, Birni, Yeni, Tondigandia, Damana, Filingué in Upper Volta and back during 5 weeks, June 24th-July 29th, 1933. Mention is made of the chief diseases observed, but for want of a microscope accurate diagnosis was at times not possible. *Dysentery* was frequent, in fact was general except at Kouré; the riverain populations are heavily infected. Much appears to be amoebic, judged by the success of emetine treatment; other forms were thought to be due to schistosomes or balantidium, not to bacilli [the need of a microscope must have been great here]. *Malaria* is present and splenic enlargement was observed in 58 out of 140 children examined, 41 per cent. A febrile condition, locally termed "hémarié" or millet fever occurs in the rainy season at the time of maturing and gathering of the millet crop. Its symptoms are characterized by sudden onset of fever with intense headache, and bilious vomiting, at times uncontrollable, and ending fatally in 2 days or so. In the majority, however, there is remission on the third day for 24-72 hours, then a return of symptoms but to a less degree. The debility is marked, but recovery takes place in 8-15 days. If there is any immunity produced it is not lasting for the patient may be attacked again the following year. As stated, if remission does not set in by the third day the fatality rate is high; on the other hand death is rare after a remission. The disease is not

epidemic ; all the cases are sporadic. There is no jaundice ; blood smears gave no clue ; the absence of jaundice, of immunity and of epidemicity and the early death in fatal cases eliminate yellow fever. There is no rash, as of dengue. Another form of fever occurs with jaundice, epistaxis, and vomiting with blood which may be Weil's disease.

Measles is an important cause of death ; *tuberculosis* not uncommon, usually of slow evolution, but in more rapid cases haemoptysis occurs. Gonorrhoea is said to be common, but gonococcal ophthalmia is rare among infants and almost any patient suffering from painful micturition was put down as a case of gonorrhoea ; many were in all probability suffering from *Schistosoma haematobium*. *Leprosy* and *syphilis* were both met with but only " moderately widespread " [no figures of prevalence are given]. *Dracontiasis* was rife, especially in the Canton of Kourfei.

[Further study of the diseases of this region might yield interesting information, particularly if investigation was aided by the use of a microscope.] H. H. S.

GEAY (M.). Étude médicale de l'annexe de Géryville. [**Medical Study of the Annexe of Géryville.**].—*Arch. Inst. Pasteur d'Algérie*. 1935. Mar. Vol. 13. No. 1. pp. 72-119. With 1 map & 7 figs. on 5 plates.

The Annexe of Géryville, situate in South Oran, measures 450 km. from north to south and 200 from east to west. In the north it is high country, in the south it is desert. The town of Géryville, a well-watered spot, is in the northern part and contains about 3,780 people, in addition to the garrison ; its climate is temperate.

Among the principal diseases observed *syphilis* takes first place. Infection is generally not venereal but due to the crowded living conditions. Primary, secondary and tertiary manifestations are described, especially the last. Nerve symptoms are very rare. Abortions are frequent and the congenital disease is common at 4 to 10 years. There have been several outbreaks of *malaria*, especially in 1930-32. The anopheles, determined by EDWARDS, are *A. hispaniola* and *A. maculipennis*. The author himself has not seen any malaria, a testimony to the measures taken by his predecessors, which consisted in drainage and filling ; quininization of children is useless. May-October is the period when the vectors breed. *Typhus* is probably always present but is only evident when epidemic. The natives fear the French prophylactic measures and conceal their cases. Preventive measures must be promptly taken on suspicion ; laboratory evidence should not be waited for. Though it is usually benign, severe and fatal cases occur in the natives. A small epidemic in 1932 consisted of ten cases, all confirmed by Weil-Felix ; three were severe, with one death, five of moderate severity and two light. The characteristic rash was seen only three times. The author observed in 6 cases studied by him REMLINGER's tongue sign, viz., the patient is unable to put out his tongue which seems to cleave to the roof of the mouth. Two other signs which never failed were conjunctival infection and staggering ; the latter lasted into convalescence. Details of prophylactic measures are given. *Trachoma* is widespread. The proportion of infected children in the schools varies from 20 to 70 per cent., the last at Géryville itself, and in adults is not much less. *Trachoma* is, however, much less common

among the purely nomadic peoples. Since March 1932 the author has diagnosed 60 cases of *tuberculosis*, 22 of the lungs, 10 of the pleura, 14 of the bones and joints, 8 visceral, and 6 meningeal. An experiment is in progress with BCG vaccine. The author says that the Algerian native, infant as well as adult, tends to present grave forms of this infection. The author goes on to the *obstetrical service*, and notes the frequency with which the French doctor is called to deliveries in native families. Details are given of the sanitary organization of the Annexe.

A. G. B.

- i. TAYLOR (H. W. Y.). **The Incidence of Certain Tropical Diseases in Moukden and the Surrounding Parts of South Manchuria.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 403–406.
- ii. HIYEDA (Kentaro). **On the Distribution of Parasites and Parasitic Diseases in Manchuria.**—*Ibid.* pp. 557–562. With 3 charts.

i. An account of the tropical diseases seen at the Mukden Hospital from 1929–1933, from a population of 16 to 20 millions.

The temperature varies from 39°C. in the shade in July to –25°C. in January. A table records the diseases with number of cases, proportion, and whether indigenous or not. The list is easily headed by trachoma which provided over 6 per cent. of cases: a long way behind comes Hongkong foot, and then dysentery, both bacillary and amoebic, and benign tertian malaria. The diseases believed to be endemic are—malaria, kala azar, relapsing fever, trachoma, dysentery, typhoid, beriberi, Hongkong foot and tinea imbricata. No cholera or plague was seen. Leprosy is not serious and it is doubtfully indigenous.

ii. The information given has been published [see this *Bulletin*, ante, p. 509.]

A. G. B.

- TAO (S. M.). **The Place of Parasitology in the Medical Curriculum in China.**—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 2. pp. 563–570. [14 refs.]

A plea is made for the provision of a place in the curriculum of all medical schools in China for the teaching of parasitology and for the establishment of a post-graduate course in tropical diseases and parasitology by the Central Field Health Station in Nanking or in one of the better equipped research institutes or schools in China. China has suffered because the curriculum followed in her medical schools is based on that of Western lands, where parasitology bulks small. A. G. B.

- BROUGHTON-ALCOCK (W.). **Further Laboratory Observations on a Large Number of Pensioners who contracted Malaria and Enteric Fevers during the Great War and returned to Residence in England.**—*Jl. Trop. Med. & Hyg.* 1935. Mar. 15. Vol. 38. No. 6. pp. 65–66.

The observations here referred to are based on the examination of more than 50,000 troops returned to Great Britain after the War and suffering from infections contracted during their service. The author, who was Director, Central Laboratory, Ministry of Pensions, refers to a previous paper [see this *Bulletin*, Vol. 18, p. 95] and writes—"I can now with emphasis repeat that malarial parasites do not remain in war

cases beyond five years after return home." Indeed after 15 months parasites were rarely found. Of those detected 787 were *P. vivax*, 14 *P. falciparum* and 5 *P. malariae*. The introduction of the Tanret test for quinine in the urine of out-patient pensioners showed that 70 per cent. were not taking it. During the year 1922 there were 46 per cent. positive Tanrets and 54 negative, so that "without being dogmatic" one may attribute recovery to home life in England and the development of immunity [? the dying out of the parasites].

In the first 5 post-war years only one enteric carrier, of *Bact. paratyphosum* A, was found and in the first 8 years only one of *Bact. typhosum*, showing that the body early rids itself of infection.

A. G. B.

BENAVIDES (Joaquin). Comments and Procedure on Thick Blood Film Technic.—*Jl. Lab. & Clin. Med.* 1934. Dec. Vol. 20. No. 3. pp. 289-295. With 2 figs.

This is a useful article describing the thick film method of blood examination for field survey work. The staining and dehaemoglobinization are carried out in blocks of 25 slides as recommended by BARBER. The article is full of practical detail and includes a very useful and simple method of preparing the Giemsa stain from Azur II eosin.

C. M. Wenyon.

PARDINA (Jose M.). Parasitosis intestinal infantil. [Intestinal Parasitism in Children].—*Prensa Méd. Argentina.* 1935. May 29. Vol. 22. No. 22. pp. 1050-1062. [79 refs.]

This was a paper read at the Fifth Medical Congress, held at Rosario and dealing with the results of laboratory examinations of the faeces of children at the Hospital, Córdoba. Altogether specimens from 505 children were examined, and the large number of 360 were found positive, 71.2 per cent.; 262 or 72.7 per cent. of those positive were passing protozoal parasites, one or more, 98 or 27.0 helminthic ova and 184 or 51 per cent. both. Of protozoa the commonest was *Giardia lamblia* in 116 or 32.2 per cent., *E. histolytica* (vegetative or cystic forms) 74 or 20.5 per cent. One hundred and sixty-one had one parasite only, 102 had more. Of the helminthic infestations *Enterobius* was the commonest, 31 or 8.6 per cent., *Hymenolepis nana* next, 24 or 6.6 per cent., then, in order, *T. saginata*, 13 or 3.6, *Necator*, 12 or 3.3, *Ascaris* and *Trichuris*, each 9 or 2.5 per cent. The majority of the patients showed no obvious symptoms as a result of the parasitism.

H. H. S.

SIMIN (N. A.). 19 Fälle von Coccidiosis bei Menschen. [Nineteen Cases of Human Coccidiosis].—*Rev. Microbiol., Epidémiol. et Parasit.* 1934. Vol. 13. No. 2. [In Russian pp. 165-167. German summary p. 167.]

The author records 19 cases of human coccidiosis (*Isospora hominis*) from Abkhasia, in Transcaucasia, found in 1931-1932. In every instance the identity of the oöcysts discovered in the stools was confirmed morphologically, by cultivation (sporulation) and by animal experiments (which were negative). In the majority of cases (13) subjective complaints and intestinal disorder were present. In several out-patients the oöcysts could be recovered in the course of four months.

C. A. Hoare.

REDAELLI (P.) & CIFERRI (R.). Affinité entre les agents de l'histoplasmosse humaine, du farcin équin et d'une mycose spontanée des muridés. [**Systemic Relations between Human Histoplasmosis, Epizootic Lymphangitis and Cryptococcus of Mice.**]—*Boll. Sezione Ital., Soc. Internaz. di Microbiologia*. Milan. 1934. Oct. Vol. 6. No. 10. pp. 376-379.

Discussing the systematic position of *Histoplasma capsulatum*, the authors conclude that the causative organism of epizootic lymphangitis of horses (*Cryptococcus farciminosus*) and *Cryptococcus muris* of mice are closely related to it and actually belong to the same genus, their names becoming *Histoplasma farciminosum* and *Histoplasma muris* respectively. The family Histoplasmaeae is one of the three subdivisions of the super-family Adelosaccharomycetaceae of Guilliermond which includes all the asporogenous fungi. C. M. Wenyon.

CHABRILLAT. Note sur la fièvre de trois jours. [**Three Day Fever.**]—*Bull. Soc. Path. Exot.* 1934. Oct. 10. Vol. 27. No. 8. pp. 762-766.

A French man-of-war was in harbour and dry dock in Madagascar on a cruise to Bombay, Calcutta and Aden ; while in harbour but also during the cruise many cases of a 3 day fever occurred, with severe headache and backache, no rash, the cases resembling sand-fly fever rather than dengue.

The cases occurred as follows :—

14th March to 8th May 1931	73 cases.
23rd December to 4th February 1932	15 "
17th March to 26th May 1932	40 "
Total	128 "

Eighty-five per cent. of the personnel were infected.

The interesting point is that in Madagascar there were few or no sand-flies and very numerous *Aedes aegypti*. The few sand-flies disappeared within 24 hours of leaving harbour but the *Aedes* remained and cases continued to occur. D. Harvey.

MATHEW (R. Y.). **Interim Notes on an Outbreak of Coastal Fever at Tully, North Queensland.**—*Health*. Canberra. 1934. Aug. Vol. 12. No. 8. pp. 54-57.

Coastal fever has occurred in certain areas in North Queensland ever since the first settlers arrived there ; other names given to the disease are " scrub " fever, epidemic glandular fever, Mossman fever. The duration of the fever varies from 3 days to 3 weeks accompanied by a general enlargement of the superficial lymph glands ; a macular rash is frequently observed.

In 1934 some 30 cases of coastal fever occurred among workers in the cane sugar plantations at Tully in N. Queensland and were investigated by the writer of this paper. Seven people out of eight in one barrack room went down with the fever and some stated that they had had similar attacks in previous years.

Clinical notes.—The disease is characterized by a sudden onset with rigor, severe headache and backache and pain behind the eyes with

flushed face ; the fever lasted for 4 or 5 days but there was no characteristic saddle back temperature curve.

Laboratory notes.—Blood culture, blood films, agglutination tests with *Bact. typhosum* and *paratyphosum* A, B, C and *Proteus* X19 and XK were all negative.

It is suggested that possibly the disease is either a form of leptospirosis or else a modified dengue. D. Harvey.

SCHARLES (F. H.) & SEASTONE (C. V.). **Haverhill Fever following Rat-Bite.**—*New England Jl. of Med.* 1934. Oct. 18. Vol. 211. No. 16. pp. 711–714. With 1 fig. & 1 chart. [13 refs.]

The description of a case of "Haverhill fever" in a medical student who was bitten by an albino rat. The bite was followed by a transitory lymphangitis, recurrent fever, associated with morbilliform rash and arthritis. Repeated blood cultures, dark field examinations of the blood, and injections of blood into mice and guineapigs were negative. Culture of the joint fluid yielded an organism which was identified as *Haverhillia multiformis* which is probably the same as *Streptobacillus multiformis*, described by LEVADITI, NICOLAU and POINCLOUX (1925).* The patient's serum agglutinated this organism in high titre.

E. Hindle.

RHOADS (C. P.) & MILLER (D. K.). **The Association of Bartonella Bodies with Induced Anemia in the Dog.**—*Jl. Experim. Med.* 1935. Jan. 1. Vol. 61. No. 1. pp. 139–148. With 1 fig. & 1 plate. [11 refs.]

On feeding splenectomized dogs on a diet which produces black tongue there developed an anaemia associated with the presence of *Bartonella canis* in the red blood corpuscles. The addition of lean beef to the diet resulted in the appearance of reticulocytes and disappearance of the parasite. Blood from an animal showing *B. canis* injected into splenectomized dogs, produced a large infection, whereas no infection was produced by injection into normal dogs. C. M. Wenyon.

MAGASIN DE PARASITOLOGIE DE L'INSTITUT ZOOLOGIQUE DE L'ACADÉMIE DES SCIENCES DE L'URSS. 1934. Vol. 4. pp. 1–367. Numerous figures and tables.

This issue of the *Magasin de Parasitologie* of Leningrad consists of fifteen contributions from various authors, of which nine at least are of interest to the medical entomologist. With one exception, which is in German, the papers are in Russian, but, again with one exception, are provided with German summaries. The titles given below are taken from the German Table of Contents, which follows that in Russian.

- i. GUZEVIČ (A. W.). Über die Stechmücken der Chibiner Berge. [On the Mosquitoes of the Chibin Hills.]—pp. 5–17. With 3 figs. and 4 tables.

Guzewiç's paper deals with a collection of mosquitoes made during the years 1930–1932 in the vicinity of Chibinogorsk, in the Kola Peninsula. No Anopheles were encountered. The prevailing species was *Aedes pullatus*, met with for the first time within the Arctic Circle,

* C. R. Acad. Sci., Vol. 180, p. 1188.

more than 1,250 miles from Saratov on the Volga, its nearest hitherto-known locality. *A. pullatus* was found to breed in very small pools in the peat, fully exposed to the sun.

- ii. PETRISCHTSCHewa (P. A.). Zur Biologie von *Anopheles bifurcatus* in Turkmenien. [**The Biology of *Anopheles bifurcatus* in Turkmenistan.**—pp. 19–30. With 8 figs. & 4 tables & charts.

Although in Palestine breeding freely in rock-cisterns, the openings into which are sometimes actually inside houses, *Anopheles bifurcatus* in Turkmenistan (Transcaspia) is stated to enter dwellings and out-houses only exceptionally. Consequently, in spite of its wide distribution in the country, the species, as a potential vector of malaria, is of extremely limited and practically negligible importance.

- iii. MARTINI (E.). Der Sowjetunion Bedeutung für das Problem der *Anopheles maculipennis*-Rassen. [**The Importance of the Soviet Union to the Racial Problem in *Anopheles maculipennis*.**—pp. 31–42. With 3 figs.

Russia may ultimately shed fresh light on the racial question in *Anopheles maculipennis*. Accordingly Martini, in the only German paper in the collection, after stating the chief points, with especial reference to the races *atroparvus*, *labranchiae*, *typicus* (*maculipennis*) and *messeae*, with which readers of this *Bulletin* must be familiar, draws attention to some present-day problems, and remarks that hitherto all our knowledge has been obtained in Western Europe. On the other hand:—"The Soviet Union, with its enormous extent from north to south, offers a vast field for study, wherein perhaps quite different forms of eggs may occur." Russia, moreover, with its many foci of malaria, should afford grounds for important conclusions as to whether highly malarious conditions occur only within the area of a particular race of *A. maculipennis* or not. Similar valuable information might be obtained as to the influence of salinity and temperature of water in breeding places, and of climate and deviation by means of cattle.

- iv. BEKLEMISCHEW (W.), in co-operation with SCHIPIZINA (N.), POLOWODOWA (W.) & NABOKICH (P.). Ueber die Genauigkeit der Abundanzbestimmung von *Anopheles maculipennis*-Larven in Pflanzenbewachsenen Gewässern. [**The Accuracy of the Determination of the Abundance of *Anopheles maculipennis* Larvae in Waters Rich in Vegetation.**] pp. 43–63. With 11 tables & 1 fig.

Again with reference to *A. maculipennis*, it is asserted by Beklemishev that every quantitative method of capture must be studied from two points of view, namely the percentage of the mosquito population, actually present, caught by the method employed, and the degree of accuracy possessed by the latter. The author, who used an ordinary gauze net and worked near Magnetogorsk, in the inundated region of the Ural River, takes as coefficient of productivity the percentage of the total number of larvae, at the moment of capture in the area under investigation, formed by those actually caught. By means of extrapolation it was found that the total number of larvae in a square metre of *Potamogeton pectinatus*, with an admixture of other plants (*Ceratophyllum*, *Myriophyllum* and *Lemna trisulca*), was 424. The coefficient of productivity of the first stroke of the net was 56·75 per cent. Four similar investigations, in growths of Canadian water-weed (*Elodea*), were carried out at different times and in different waters, when,

although larval abundance differed greatly in the four cases, the mean corresponding coefficient proved to be 54.6 per cent. Although the regularity of their distribution varies in different plant-communities, the larvae abound in thick growths of *Elodea*. It is claimed in conclusion that there is urgent need of further investigations into the productivity and accuracy of different methods of capture, in different conditions. Only so will it be possible to introduce critically tested standards, and thus, in respect of larval oecology, to raise practical malariology to a higher level.

- v. MONTSCHADSKY (A.). Über das Wachstum und die Funktion der Analkiemien bei den Larven von *Anopheles maculipennis* Mg. [**The Growth and Function of the Anal Gills in the Larvae of *Anopheles maculipennis*.**—pp. 65–83. With 6 tables & 5 graphs.

Though concerned with larvae of *Anopheles maculipennis*, Montschadsky's paper is mostly outside the scope of this *Bulletin*. According to its author, the object of this highly technical article is to emphasize the need for experimental reconsideration of the function of the anal gills. There are grounds for thinking that the office of the anal gills is not confined to breathing, but is rather of an excretory nature, or has even to do with the regulation of osmosis.

- vi. BURAKOVA (L. W.). Zur Methodik der Untersuchung und des Nachweises der *Phlebotomus*-Arten. [**The Method of investigating and demonstrating the Species of *Phlebotomus*.**—pp. 93–98.

Beyond suggesting that, in places in which collecting by ordinary methods is difficult, the presence of sand-flies may be demonstrated by the aid of "tanglefoot," this short paper relating to *Phlebotomus* appears to include little of special interest.

- vii. PAVLOVSKY (E. N.), STEIN (A. K.) & BYTSCHKOV (W. A.). Experimentelle Untersuchung der Wirkung des Speichels der Larve von *Calliphora erythrocephala* auf die Hautdecke des Menschen. [**The Effect of the Salivary Secretion of the Larva of *Calliphora erythrocephala* upon the Human Skin.**—pp. 99–110. With 4 figs. & 1 table.

In connexion with the use of maggots in the treatment of osteomyelitis and other maladies, the authors tested the action of the salivary secretion of larvae of *Calliphora erythrocephala* (the common blowfly) and *Musca domestica* on the normal human integument. The salivary glands of the former, after removal from living adult larvae, were emulsified in physiological solution, and the emulsion was injected subcutaneously into man. The injection produced an inflammatory reaction in the form of a vesicle, which subsequently became an urticating papilla; these effects passed off on the second or third day. The salivary secretion of larvae of *Musca domestica* behaved in a similar manner, but its effects were more transient. The active principle of the salivary secretion of the larvae of *C. erythrocephala* is unaffected by heat.

- viii. TINKER (J. S.) & SENKEWITSCH (M. A.). Einige Beobachtungen in Bezug auf die Ökologie der Zieselmausflöhe im Zusammenhang mit ihrer Rolle in der Epidemiologie der Pest. [**The Oecology of Suslik Fleas in Connexion with their Rôle in the Epidemiology of Plague.**—pp. 203–215. With 3 figs. & 2 tables.

The flea parasites of the suslik (*Citillus citillus*) do not remain permanently on their hosts or in their burrows, but make nocturnal

excursions to the outer world and return to the burrows by day. When pads of loose wadding, two to each hole, were introduced into burrows, a pad inserted in the morning being left for varying periods of time up to twelve hours, the other being allowed to remain throughout the night, fleas were subsequently found on the outside of the morning pad, which was close to the surface of the ground, but on the inner side of the other and lower pad. It thus appears that the fleas congregate above ground at night, which is therefore potentially the more dangerous period, provided that the insects contain the plague bacillus. On the surface of the ground near suslik holes, on six occasions, the authors collected in all 190 free-living fleas belonging to the species *Neopsylla setosa* and *Ceratophyllus tesquorum*.

- ix. ZOLOTAREV (N. A.). Zum Artenbestand und zur geographischen Verbreitung der Zecken (*Ixodidae*) in Dagestan. [**The Species of Ticks (*Ixodidae*) in Daghestan and their Geographical Distribution.**]—pp. 217-227. With 2 charts.

Although this paper on the ticks of Daghestan (Caucasia) is unfortunately not provided with the usual German summary, the numerous lists of species, being printed in ordinary italics, are readily intelligible.
E. E. Austen.

- LAMBORN (W. A.). **Annual Report of the Medical Entomologist for 1934.**—*Nyasaland Ann. Med. & San. Rep. Year ending 31st December, 1934.* Appendix I. pp. 65-69.

Dr. Lamborn's report gives as usual an account of interesting and well devised observations and experiments.

He made tsetse fly surveys in the Dowa and Fort Manning Districts in the Northern Province and expresses the opinion that the position as regards fly in these regions remains satisfactory. He visited also the shore of the Lake in the Dowa district where a township is projected at the head of the railway. Here tsetse swarmed as twenty years ago when the Sleeping Sickness Commission of the Royal Society was there. He learnt that a large acreage for cotton growing had been applied for by Europeans and thinks that this cultivation will go far to reduce the fly menace; he therefore does not advise any special measures for fly reduction.

He gives an account of the researches made by J. G. THOMSON and himself on mechanical transmission of trypanosomiasis, leishmaniasis and yaws by blood-sucking non-biting flies [*ante*, p. 68]. When THOMSON left Lamborn endeavoured to ascertain whether *L. donovani* and *L. tropica* can undergo cyclical development within *Musca spectanda*, the fly which was used in the joint experiments. He fed the flies on cultures of leishmania and then allowed them to feed at scratches on the ears of experimental dogs [number not stated]. None of the animals showed signs of infection. Many of the flies were dissected but leishmania were not found. "I had indeed little expectation otherwise since the flagellates do not occur in the cultures in the resting phase in which they must normally be ingested by an insect vector."

Other observations were concerned with leprosy. The author wished to find out to what extent *M. sorbens*, which seems to select the foulest of sores for feeding, ingests and passes the leprosy bacillus. He examined the faecal deposits of bred flies fed on a leprosy sore. Up to 2 days all were positive, on subsequent days 32 out of 71, 6 out of 17,

3 out of 36, 20 out of 44 ; on the 10th day 1 out of 24 and on the 13th 1 out of 16. He considers that his evidence tends to show that *M. sorbens* may be the transmitting agent of acid-fast bacilli present in a leprous sore, through its vomit drop or excreta. Passage through one of these flies may be necessary to activate the organism and make it infective, its capsule undergoing partial solution perhaps, for simple implantation of the bacillus does not produce infection. He thinks that the rôle of Muscids in the transmission of leprosy has been little explored. Other observations concerned Tabanidae. A. G. B.

BLACKLOCK (D. B.). **Screencloth for Houses in the Tropics.**—*Ann. Trop. Med. & Parasit.* 1935. July 17. Vol. 29. No. 2. pp. 261–263.

This paper makes practical proposals for the reduction of the cost of screencloth as wire gauze is technically called.

The author points out that the chief factor in maintaining the price of screencloth has been the irregular orders for this material specifying many different meshes, and gauges of wire. So long as manufacturers have to set up and adjust machines—a very costly item—to produce a large variety of sizes of mesh, and use wire of different gauges, the cost of the material is bound to remain high. Whereas if requisitions of screencloth were standardized to one or two types, there would be a great fall in the cost of production.

He advises, therefore, the adoption of *MacArthur's recommendations to employ for buildings screencloth of 14 meshes to the linear inch, woven of wire of no. 30 Imperial Standard Wire Gauge ; and for screening water tanks, etc., an 18-mesh screencloth of 30 I.S.W.G. The reason for advocating a finer mesh for the latter purpose is that freshly-emerged mosquitoes might be able to force their way through a coarser mesh before their chitinous exo-skeleton has finally set. Blacklock suggests that for screening water-containers where, unlike houses, the exclusion of light is immaterial, a stouter wire—*i.e.*, 28 I.S.W.G. would provide a more durable material.

One of the newer metal compositions, a British product known as Barronia metal, is strongly recommended by the author. To his knowledge, screencloth made of this material was fixed in the windows of an animal house in the exacting climate of Sierra Leone, where it remained quite unprotected from the weather for well over two years. At the end of this trial period the wire was examined and was found to show no signs of wastage or corrosion. Barronia wire does not require painting as the slight film which forms on the wire from weathering acts as a protective covering and increases the resistance to corrosion. Another strong point in favour of Barronia is that its cost is only some two-thirds that of Monel metal. W. P. MacArthur.

McMAHON (J. P.). **Preliminary Notes on the Control of Flies.**—*East African Med. Jl.* 1935. Aug. Vol. 12. No. 5. pp. 128–135. [Summary appears also in *Bulletin of Hygiene.*]

The paper discusses flies coming from sanitary traps, pit latrines, etc., in Nairobi : also the possibility of using repellents.

The enquiry arose because of the abundance of *Musca* in parts of Nairobi, and it was easy to show that they came principally from the

*Sanitation Supplement of *Trop. Dis. Bull.*, 1923, p. 12.

area in which night-soil was deposited and buried in rather shallow trenches. The very familiar objections to this system of disposal are set forth. It was found also that a considerable number of flies were coming from pit latrines. Apparently these are deep, but not dark or fly-proof. The author states that naphthalene was occasionally successful as a repellent, but that he got more complete and consistent results with paradichlorobenzene in powder form. He put about 2 lb. of this in a pit latrine when he started operations, and after that reduced his application to 4 oz. once a week.

It is clear that the members of the group of house-flies very closely related to *Musca domestica* differ from one another in points of anatomy and of behaviour. The majority of those bred from Nairobi are apparently a new species, the description of which by PATTON is in the press. It is quite possible that this species cannot be controlled by methods which are so successful in West Africa, but we suggest that the authorities in Nairobi might experiment with the Otway pit. The paper states that considerable numbers of *Lucilia sericata* were bred from some of these deposits of faeces: that may be so, but is the identification correct? Small green *Chrysomya* commonly breed in such places in tropical countries.

P. A. Buxton.

SALEM (H. H.). **Myiasis in Egypt.**—*Jl. Egyptian Med. Assoc.* 1935. Apr. Vol. 18. No. 4. pp. 238-254.

Though largely a compilation of published statements on myiasis elsewhere than in Egypt, this paper contains a modicum of original matter. Ocular myiasis, usually due to larvae of *Wohlfahrtia magnifica*, is the commonest condition within the limitations of the title, especially in Cairo and lower Egypt; from Upper Egypt it has so far not been reported. Larvae of *Sarcophaga dux* var. *exuberans* have likewise been met with (in one instance) in the human eye, and also in the ear. A particularly interesting case was that in which larvae of three different species of flies—*Eumerus vestitus* (which normally breeds in decaying onions), *Musca domestica* and *Piophilala casei* (the "cheese maggot" fly)—issued from the ear of a child suffering from otorrhoea. Two cases of intestinal myiasis caused by *Sarcophaga hirtipes* and *S. dux* var. *exuberans* have been observed by the author, who, however, has yet to meet with the much rarer condition known as urinary myiasis.

E. E. Austen.

JOBLING (B.). **The Effect of Light and Darkness on Oviposition in Mosquitoes.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. July 31. Vol. 29. No. 2. pp. 157-166. [9 refs.]

The paper describes experiments, the purpose of which is to define the conditions under which female *Culex* most readily lay eggs: in particular the degree of illumination is selected for study.

In spite of the fact that egg-rafts of *Culex* are nearly always deposited at night, it is clear from observations in the field that the female prefers a water which is shaded to one freely exposed to what little light there may be. For instance, in cage experiments more egg-rafts were laid in a Petri dish standing on black paper than in one standing on white paper. A very little shading of the water surface caused it to be chosen by female *C. pipiens* of the autogenous race, provided they had had a meal of blood: those which had had no meal showed no discrimination, the whole experiment being performed twice with consistent results.

Having shown that hay infusion was much more attractive than water to his insects, the author experimented with those two liquids, shading the water with a paper collar: the great majority of females still chose the hay infusion.

It would be of interest if the work could be extended, a controlled illumination of very low intensity being used, and measured at the water surface.

P. A. Buxton.

BUXTON (P. A.). Changes in the Composition of Adult *Culex pipiens* during Hibernation.—*Parasitology*. 1935. May. Vol. 27. No. 2. pp. 263-265. With 1 fig.

In *Culex pipiens* as in *Anopheles maculipennis*, both of which hibernate as adults, there is a characteristic autumnal accumulation of fat, which gradually disappears as winter progresses. As to the amount of fat stored up, and its rate of disappearance, knowledge is lacking. The author's observations were made on adult female *C. pipiens*, collected in a cellar in Kent "at intervals from September to April in the years 1930-4." After being killed and weighed, the insects were dried to a constant weight at 105°C., and treated with ether, it being assumed for experimental purposes "that what is lost at 105°C. is water, and what dissolves in ether is fat," though "neither assumption is strictly accurate." It appears that "As hibernation proceeds, there is a gradual reduction in the female's total weight from over 3 to under 2 mg."; and that "Towards the end of hibernation, particularly in March and April, the figure for fat is very low, falling to about one-seventh of what it was in September and October. . . . The solids other than fat show remarkably little change in weight during the period of hibernation. . . .", though a great rise occurs in the proportion that they bear to the whole. With the progress of hibernation "the weight of fat decreases more rapidly than that of water," the proportion of which "rises during hibernation." It may be assumed that "as the fat disappears, the space which it occupied is partly filled by increasing the amount of air in the diverticula, so that the insect's loss of weight is greater than the reduction in its size."

E. E. A.

KEILIN (D.), TATE (P.) & VINCENT (M.). The Perispiracular Glands of Mosquito Larvae.—*Parasitology*. 1935. May. Vol. 27. No. 2. pp. 257-262. With 2 figs. [13 refs.]

Glands producing an oily secretion, such as have been described by KEILIN and others in the larvae of many Diptera, are here described in detail in Culicine and Anopheline mosquitoes. In both groups they lie close to the spiracular opening, and are clearly responsible for the differential wetting of the spiracular region which permits oil but not water to enter the tracheal system.

V. B. Wigglesworth.

TRAGER (William). The Culture of Mosquito Larvae Free from Living Microorganisms.—*Amer. Jl. Hyg.* 1935. July. Vol. 22. No. 1. pp. 18-25.

———. **On the Nutritional Requirements of Mosquito Larvae (*Aedes aegypti*).**—*Ibid.* Sept. No. 2. pp. 475-493. [25 refs.]

The larvae of *Aedes aegypti* require at least two growth-promoting substances.

One of these is present in large amounts in yeast and aqueous yeast extract, in egg white and in wheat. It is heat- and alkali-stable and is not adsorbed by fuller's earth; it seems to belong to the "B" group of vitamins. The other, present in large amount only in partly purified liver extracts, may perhaps be related to the anti-pernicious anaemia factor. Both factors are provided by living bacteria or yeasts.

V. B. Wigglesworth.

YANG (Foo-Hai). Zur Kenntnis der Phlebotomen-Arten in China und zur Aetiologie des Phlebotomen-fiebers. (Mit einem Anhang ueber die Verbreitung des Insekts in China.) [**Species of Phlebotomus in China; their Prevalence and Part played in the Aetiology of Sand-fly Fever.**].—*Far Eastern Assoc. Trop. Med. Trans. Ninth Congress, Nanking, China, 1934.* Vol. 1. pp. 495–502. With 6 figs. on 1 plate & 1 map. [20 refs.]

There are three species of phlebotomus which have been associated with sand-fly fever in China. The author discusses the differentiation of these by means of a special study of the male generative organs. He also gives a map showing the distribution of these species. He attempted by means of tissue culture experiments, using some of the newer methods employed in the culture of Rickettsia, to isolate a germ but without any result.

D. Harvey.

OHMORI (Nanzaburo). **Experimental Studies on the Influence of Low Temperatures upon the Tropical Bed-Bug (*Cimex hemipterus* Fabricius). Second Report. On the Influence of a Temperature of 3°C.**—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa).* 1935. June. Vol. 34. No. 6 (363). [In Japanese pp. 702–713. With 1 fig. [21 refs.] English summary pp. 714–715.]

The paper is an extension of one previously noticed (*ante*, p. 670). The author has bred tropical bedbugs (*Cimex rotundatus*) at 27°C. and then exposed them to 3°C., bringing them back to 27°C. to observe the effect of low temperature. He finds that at 3°C. the eggs are not affected by an exposure of 3 days, that nearly all are killed after 15 days, and all after 20 days. Moreover, eggs that have been recently laid will survive this temperature for a longer period than eggs which are 2–4 days old at the beginning of the experiment. A range of experiments with nymphs and adults, fed and unfed, is also recorded. At all stages the insect shows considerable powers of resistance to this low temperature, and this is surely remarkable in view of its restriction to warm parts of the globe.

P. A. Buxton.

FERRIS (Gordon Floyd). **Contributions toward a Monograph of the Sucking Lice. Part VIII.**—*Stanford Univ. Publ., Univ. Ser. Biol. Sci.* 1935. Vol. 2. No. 8. pp. 529–620. With 3 plates & 33 text figs.

This work is the final part of an important monograph which began to appear in 1920. The present part is mostly concerned with *Pediculus* and *Phthirus*.

Professor Ferris confines himself rather strictly to matters of anatomy and systematics. Under each genus he gives a full synonymy and definition of the anatomical characters of the genus. In the case of

Pediculus, this is followed by a synonymy of the species which have at some time been referred to it (many of which are not sucking lice at all), and by a selected bibliography. The author has examined a very large amount of material from human beings in all parts of the world, and discusses two vexed questions: the distinctness of head and body lice, and the existence of particular races of lice on certain races of man. After a very detailed examination of the external anatomy, he concludes that no point of difference exists by which head and body lice may be separated with confidence, though he observes that certain strains exist in nature "in which the typical characteristics that are supposed to define these two forms are clearly developed." The two forms are referred to as *capitis* and *corporis*, but the author refuses to give them formal recognition even as subspecies. He points out, quite correctly, that the experimental evidence on hybridization and on adaptation to changed environment, though incomplete, points to the same conclusion.

Turning to the question of lice from different races and to the study of the so-called species which have been described, Professor Ferris finds no points of difference except in *maculatus* Fahrenholz, which occurs on negro races; even this form, which is typically distinguishable by small size, compact shape and dark colour, shows no sharp anatomical points of distinction and inter-breeds completely with head lice and body lice from other races of man.

The points here discussed have considerable interest outside pure taxonomy. Specimens and literature have been fully considered by a great authority on the anatomy of biting lice, and his conclusions do not differ greatly from those arrived at by Nuttall nearly twenty years ago. Now that the anatomists have failed to find constant reliable differences between head louse and body louse, we may perhaps assume, until the contrary is proved, that they are equally effective as vectors of micro-organisms. [May we also hope that examiners who continue to ask candidates to repeat an out-worn creed about the differences between these insects may be led to knowledge of the truth?]

P. A. B.

HERMS (W. B.), BAILEY (S. F.) & McIVOR (B.). **The Black Widow Spider.**—*Bull. Calif. Agric. Exp. Sta.* Berkeley, California. 1935. June. No. 591. 30 pp. With 14 figs. [24 refs.] [Summarized in *Rev. Applied Entom.* Ser. B. 1935. Sept. Vol. 23. Pt. 9. p. 212.]

"The increase in the number of reported cases of bites by the poisonous Theridiid, *Latrodectus mactans*, F., is thought to be due to more accurate diagnosis and to the gradual adaptation of the spider to living in shelters erected by man.

"Notes are given on its distribution, morphology and bionomics, and the nature of its venom, its effect on laboratory animals and man, and the treatment of bites in the latter are discussed. Owing to its wide distribution, solitary habits and varied habitat, it is difficult to control. It almost invariably recovers from the effects of fly sprays but is killed when sprayed directly with creosote, which also acts as a repellent. Only three natural enemies are known, *viz.*, the Scelionid, *Baeus latrodecti*, Dozier, which was taken in Haiti and is a true egg parasite (a single larva killing a single egg), and a Chloropid and a species of *Gelis*, which were observed in California feeding on the eggs in the egg-sac and destroying complete broods."

FRAWLEY (J. M.) & GINSBURG (H. M.). **The Diagnosis and Treatment of Black Spider Bite.**—*Jl. Amer. Med. Assoc.* 1935. May 18. Vol. 104. No. 20. pp. 1790-1792.

In the last 7 years 52 cases of black spider bite (*Latrodectus mactans*) have been treated at Fresno, California. The chief symptom is severe pain over the abdomen and rigidity of the abdominal muscles. No deaths have resulted. The patients are treated thus :—

" 1. The patient is immediately put to bed and iodine is applied to the site of the bite.

" 2. A soapsuds enema is administered, and fluids are given freely by mouth.

" 3. Morphine sulphate is given hypodermically to control the pain and sodium amylal to insure rest.

" 4. Magnesium sulphate, a 20 cc. ampule of 10 per cent. solution, is given intravenously, to be repeated as required to overcome the hypertension and the spasticity of the muscles.

" Results with this form of treatment have been very satisfactory. Last summer we used it in eleven cases. It was never necessary to give more than one dose of magnesium sulphate. The patients were usually free from symptoms within twenty-four hours." A. G. B.

BRUNON (Roger). Notes sur l'hygiène publique en Afrique noire. Soleil et nudisme. Régimes alimentaires. Logement. Sport et culture. Hygiène morale.—*Ann. d'Hyg. Pub., Indust. et Sociale.* 1935. July. Vol. 13. No. 7. pp. 386-395.

CASTRONUOVO (Giovanni). Malattie dominanti in Abissinia e loro prevenzione.—*Giorn. Ital. di Malat. Esot. e Trop.* 1935. June 30. Vol. 8. No. 6. pp. 139-142, 145-148, 151-154.

CRAIG (Charles F.). Theobald Smith and the Insect Transmission of Disease.—*Amer. Jl. Trop. Med.* 1935. July. Vol. 15. No. 4. pp. 407-414.

DREYFUS (M.). Observation de myiase des voies lacrymales à sarcophaga.—*Rev. Méd. et Hyg. Trop.* 1935. May-June. Vol. 27. No. 3. pp. 114-115.

GUZEWITSCH (A. W.) & PODOLJAN (W. J.). Die Pyrethrum-Rauchlichter als Bekämpfungsmittel der Stechmücken und der Phlebotomen.—*Rev. Microbiol., Epidémiol. et Parasit.* 1935. Vol. 14. No. 1. [In Russian pp. 87-98. With 1 fig. German summary p. 98.]

LINDSAY (John W.). Medical Services in the Chaco War.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. Apr. Vol. 28. No. 6. pp. 539-558. With 2 maps.

A very interesting address, not suitable for summary.

MANSON-BAHR (Philip). A Commentary on the Diary kept by Patrick Manson in China and now conserved at Manson House.—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1935. June 29. Vol. 29. No. 1. pp. 79-90. With 1 plate.

MASSIAS (Charles). Myosites suppurées observées en Cochinchine.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1935. Feb.-Mar. Vol. 13. No. 2. pp. 83-86. [11 refs.]

MAZZOLANI (D. A.). Pseudo-emottisi irudinea in Tripolitania.—*Policlinico. Sez. Prat.* 1935. Aug. 19. Vol. 42. No. 33. pp. 1634-1641. [32 refs.]

PALIT (A. N.). Splenectomy for Tropical Splenomegaly.—*Indian Med. Gaz.* 1935. May. Vol. 70. No. 5. pp. 243-247. With 1 fig.

PERVÈS. Observations de météorologie médicale recueillies pendant les années 1933 et 1934 à Tamanrasset (Hoggar).—*Bull. Acad. Méd.* 1935. June 4. 99th Year. 3rd Ser. Vol. 113. No. 21. pp. 809-813.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH. Annual Report by the Curator of the Laboratory for the Year 1934 [PHILIP (Robert)].—25 pp.

VON SCHUCKMANN (W.). Ueber das Vorkommen tierischer Entoparasiten beim Menschen in Deutschland.—*Reichs-Gesundheitsblatt.* 1935. June 26. Vol. 10. No. 26. pp. 571-574. [17 refs.]

STANNUS (Hugh S.). The Care of European Children in the Tropics.—Reprinted from *Practitioner.* 1935. Aug. Vol. 135. pp. 138-145.

REVIEWS AND NOTICES.

WHITFIELD (F. G. Sarel) [F.R.E.S., F.R.M.S., Entomologist to the Sudan Government, Wellcome Tropical Research Laboratories, Khartoum, etc.] & WOOD (A. H.) [M.A. (Cantab.), Entomologist to the Gezira Agricultural Research Service, Sudan Government]. **An Introduction to Comparative Zoology. A Text-book for Medical and Science Students.** With a Foreword by Maj. Sir Robert ARCHIBALD, C.M.G., D.S.O., M.D., Late Director, Wellcome Tropical Research Laboratories, Sudan Government, Khartoum.—pp. x+354. With 141 illustrations. 1935. London: J. & A. Churchill Ltd., 40, Gloucester Place, Portman Square. [15s.]

The vigorous style of this volume, with its many similes calculated to appeal to the young student, would by itself suggest the work of a teacher—even without the summaries scattered through the book, the elaborate comparisons, and the warnings against pitfalls such as the two uses of the word plasmodium. (It might have been pointed out that in one case it is written with a capital and in the other with a small letter.) Teachers may, however, not be good writers of textbooks, and whether this is a good one or not is a matter of opinion.

Its avowed and excellent object is to provide a wide zoological basis on which might be built any superstructure of specialized Biology, academic or applied. (There is, however, a distinct bias towards the latter.) Hence the extensive classifications, and the chapters on Metabolism, Heredity, Evolution and Ecology. It is good to find allusion to certain matters of very general interest which are often omitted, such as the tadpole of the Frog, and, under Dogfish, to cod liver oil and mermaids' purses. The special reference to the choice of examples "occurring more or less universally" seems to have resulted merely in omission of details concerning the Crayfish (for which there is something to be said on other grounds) and in putting in the Locust as a second insect, although there are surely Cockroaches wherever there are likely to be classes in Zoology. Otherwise there are the usual "types" of the elementary course. Beside these are given more or less detailed accounts of selected organisms of medical or veterinary importance. In such a company it is rather surprising that Hookworms and Leeches, for example, should not be recognizably mentioned. Would it not have been advisable to use otherwise the space devoted to Sponges (with no labelled figures), to the Locust (with no account of its migrations), to the Adelochorda and Urochorda, to the disagreements of various workers about the minute anatomy of the schistosome cercariae, and to tables of classical names with no clue as to the nature or importance of the animals designated?

It is not an easy book for an elementary student to use, wherein might possibly lie much virtue. Much diligence, for example, would be necessary for him to discover exactly what is meant by the "double line" in Table 1; perseverance and some daring to trace out the meaning of "metamorphosis" when he meets this term on pp. 57 and 104; ingenuity might connect *Schistosoma* of the figures and tables with the "human blood flukes" of the text, and so on. Those who worked out some of the elaborate and obscure figures (such as nos. 26c, 78, 93, 100, 104, 108) should know something of their subject. (Suggestive letters are more helpful on a diagram than numbers, and too often.

there is no reference to the figures in the text.) But how many students would rise to the occasion? And the reviewer for one would be completely baffled in an attempt to find out the approximate dimensions of many of the Protozoa, of most of the Worms, eggs, etc. (which to one in the elementary stage might be almost any size); or to obtain any idea of a "Trochophore" (p. 21), of the "Hirudinea" (p. 23), of the Pseudophyllidea (p. 74), or of "Cyclops" (p. 75) for example.

It is perhaps a pity that two specialists in the same branch of Zoology should have collaborated in this general work. As they would probably say, it must have been "extremely" difficult to avoid making unusual statements in other branches, such as should have no place in an elementary textbook unless attention is especially drawn to them: statements such as that red blood corpuscles are the "chief source of food" of *Entamoeba histolytica*; that *Euglena* can "perform slow slug-like movements, similar to the less active movements of the Amoebae" and feeds holozoically; or that *Amoeba proteus* "sometimes undergoes a process known as plasmogamy . . . into a single mass containing several nuclei . . . known as a plasmodium." These are a few examples taken from the Protozoa.

The reviewer submitted the large entomological section to a teaching colleague who is a specialist in this subject; and it is disappointing to find even here inaccuracies and inadequacies both in text and figures, some of which might be very misleading.

The book is well produced, and very moderate in price, and many of its weaknesses could be remedied in another edition. In view of this possibility it is pointed out that there are a good few misprints in addition to those noted at the beginning of the introduction.

Margaret W. Jepps.

SOEGIRI. Bijdrage tot de kennis van de primaire longinfecties en van de frequentie der tuberculose in Indië. [Primary Tuberculous Infections of the Lungs and the Frequency of Tuberculosis in the Netherlands Indies.] [Thesis for Doctorate of Medicine, School of Medicine, Batavia.]—174 pp. With 155 figs. (6 on 4 plates). [62 refs.] 1935. Batavia-C. Drukkerij Centrum. [Review appears also in *Bulletin of Hygiene*.]

This thesis for the M.D. degree, School of Medicine, Batavia, deals with the question of pulmonary tuberculosis purely from the aspect of morbid anatomy as revealed by post-mortem examination of 256 bodies, 159 adult and 13 young Malays, 51 adult Chinese and 27 Chinese children, 5 Europeans, and 1 negro. The findings need not be detailed here; they were similar to what has been found elsewhere, notably by BLACKLOCK in Great Britain (see *Bull. of Hyg.*, 1933, Vol. 8, p. 44) and SCOTT in Hongkong (*Ibid.*, 1931, Vol. 6, p. 341 and this *Bulletin*, Vol. 19, p. 405) whose results have been issued as Medical Research Council Special Reports.

The author concludes that primary tuberculous lung infections in adults in Batavia are recently acquired. He notes the finding of well-defined fibrous lesions in the lymphatic glands sometimes with calcified, fibroid or active changes in the lung. "In some cases," he states "there is no sign of any lung lesion"; seeing that his thesis deals with primary tuberculous infection of the lungs, the meaning of this absence

of-lesion is dubious. He considers these fibrous gland lesions "as specific regressive lesions, some of them may almost attain complete restitutio ad integrum." Either the lung has achieved this complete restitutio or the gland is not infected secondarily to the lung, but this does not appear to be discussed. Perhaps the author is not at home with English literature on the subject, for though 62 references are appended no mention is made of any British workers who have probably done as much as any on this interesting aspect of the disease.

H. H. S.

GHOSH (Birendra Nath). **A Treatise on Hygiene and Public Health with Special Reference to the Tropics. Eighth Edition.**

This book was reviewed in the *Bulletin of Hygiene*, 1935, Vol. 10, p. 684.

INDEX OF AUTHORS OR SOURCES.

The bracketed abbreviations after the page numbers indicate the subjects.
Page numbers within brackets indicate papers not summarized.

Am. signifies Amoebiasis and Amoebic
Dysentery.
Bb. " Beriberi and Epidemic Dropsy.
Bl. " Blackwater.
B.R. " Book Review.
Chl. " Cholera.
C.Bu. " Climatic Bubo and Lympho-
granuloma Inguinale,
Der. " Tropical Dermatology.
Dys. " Dysentery (Bacillary and
Unclassed).
Fev. " Fevers.
Hel. " Helminthiasis.
Hist. " Historical.
H.S. " Heat Stroke.
K.A. " Kala Azar.
Lep. " Leprosy.

Lept. signifies Leptospirosis.
Mal. " Malaria.
Misc. " Miscellaneous.
Oph. " Tropical Ophthalmology.
Pel. " Pellagra.
Pl. " Plague.
Rab. " Rabies.
R.B.F. " Rat-Bite Fever.
R.F. " Relapsing Fever and other
Spirochaetoses.
Sn. " Venomous Snakes and Snake
Venoms.
Sp. " Sprue.
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 —, Franke, M. & Alexa, E., with Agapi, C., Pupu, E. & Manoliu, E., 745 (Mal.)
 —, with Slatineanu, Balteanu, Alexa, E., Alexa, I., Francke & Rugina, 411 (Mal.)
 Clarebout, G., with Mouchet, van Hoof, Duren, Fornara, Henry & Henrard, 280 (Y.F.)
 Clark, H. C., 107 (Mal.), 512 (Misc.)
 —, with Grayson & Martin, (532) (Misc.)
 —, with Komp, 434, 784 (Mal.)
 Clarke, L. P., with Findlay, 289, 290, 590 (Y.F.)
 —, with — & Hewer, 291 (Y.F.)
 Clarkson, L. M., (146) (Mal.)
 Clements, F. W., (532) (Misc.)
 Clemesha, W. W., 399 (Mal.)
 Clunie, T. & Eva, A., 519 (Misc.)
 Cluzet, with Grimes & Minec, 869 (Lep.)
 Cochrane, R. G., 538, 541, (873) (Lep.)
 Cohen, H., 899 (Oph.)
 Colarizi, A., 481 (K.A.)
 Colas-Belcour, J., 223 (Misc.)
 Cole, H. I., 548 (Lep.)
 Coleman, G. E., 299 (R.F.)
 Colichón, H., with Franco, 600 (R.B.F.)
 Collignon, E., 99 (Mal.)
 Collins, R. K., 116 (Mal.)
 —, with Drensky, 106 (Mal.)
 Comaroff, R., with Kligler, 715 (S.S.)
 Compagnini, G., 136 (Mal.)
 Conforto, A. V., with Dopff, (170) (Fev.)

Congo Belge, 501, 503 (Misc.)
 Connery, J. E., with Curran & Goldwater, (674) (Misc.)
 Connolly, M., 241 (Hel.)
 Constantinescu, N., with Ciuca & Balteanu, 559, 565 (Fev.)
 —, with Parvulescu & Boeriu, 750 (Mal.)
 Conte, M., with Rathery & Dérot, (493) (K.A.)
 Contos, B., with Caminopetros, Pheloukia & Pagonis, 575 (Fev.)
 Copeland, A. J., 733, (752) (Mal.)
 Cordiner, G. R. M., with Low, 672 (Misc.)
 Cordoliani, S., with Sautet, 406 (Mal.)
 Corkill, N. L., 465 *bis* (Pel.)
 Cormack, R. P., (532) (Misc.)
 Corman, 826 (Bl.)
 Corman, A., 743 (Mal.)
 Cornejo, A., (371) (S.S.)
 Corradetti, A., 443 (Mal.)
 Corson, J. F., 30, 33, 352 *bis*, 353, 363, 709, 710 (S.S.)
 Cort, W. W., with Foster, 641 (Hel.)
 Corteggiani, E., with Gautrelet & Halpern, 379 (Sn.)
 Cossa, with Augier, 576 (Fev.)
 Costa Mandry, O., with Suarez, (675) (Misc.)
 Coulogner, 81 (K.A.)
 Courel Fernández, M., (444) (Mal.)
 Coutinho, A., 894 (Y. & S.)
 Covell, G., 428, 441 (Mal.)
 — & Bailly, J. D., 93, 399 (Mal.)
 Crabtree, J. A., with Meleney, 107 (Mal.)
 Craig, C. F., 105, (146) (Mal.), (198) *bis* (Am.), 301 (B.R.), (915) (Misc.)
 Crane-Lillie, M. & Rhoads, C. P., 469 (Pel.)
 Creagh, E. P. N., (198) (Am.)
 Cross, S. X., with Foster, 265 (Hel.)
 —, with Landsberg, 641 (Hel.)
 Cruz, M. C., 872 *bis* (Lep.)
 Cruz, W. O., 261, 262, 640 (Hel.)
 Cuboni, E., 379 (Sn.)
 Culbertson, J. T. & Strong, P. S., 360 (S.S.)
 Cullom, M. M., 896 (Oph.)
 Cumming, J. G., 167 (Fev.)
 da Cunha, A. M., 582 (Fev.)
 Curran, J. A., Connery, J. E. & Goldwater, L. J., (674) (Misc.)

D

Damboviceanu, A. & Soru, E., 461 (Chl.)
 Dàng-Hanh-Kiên, 400 (Mal.), 827 (Bl.)
 Datta, S. K., with Banerjee, 764, (772) (Chl.)
 Dau, H., with Pijper, 154, 561 (Fev.)
 Davies, J. R., 672 (Misc.)
 Davey, T. H., with Gordon & Peaston, 237 (Hel.)
 Davidson, H. S., with Riesman, 4 (Bb.)
 Davis, G. E., 569 (Fev.)
 Davis, N. C., 126 (Mal.), 648 (Hel.)
 Dawson, J. R., Jr., with Webster, 608 (Rab.)
 De, M. N. & Chatterjee, K. D., 272 (Hel.), 490 (K.A.)
 DeBailey, M. E., with Hinman & Faust, 277 (Hel.)
 DeCoursey, E., 363 (S.S.)
 Decourt, J. & Ariès, C., 492 (K.A.)

- Decourt, P., 785, 786 (Mal.)
 Degotte, J., with Dubois, 341 (Lep.)
 —, with — & Westerlinck, 546, 870, 873 (Lep.)
 Deimer, J. H., 835 (B.R.)
 De la Barrera, J. M. & Arzeno, M., 447 (Pl.)
 De la Camara, P., (370) (S.S.)
 Delanoë, E., 869 (Lep.)
 De la Plaza, G., Vegas, M. & Gomez, B., 871 (Lep.)
 Delbove, P. with Mesnard, 157 (Fev.)
 —, with Ragiot, 157, 562 (Fev.)
 —, with — & Tran-van-Tu, 157 (Fev.)
 Del Rosario, F., with Shah & Rozeboom, 425 (Mal.)
 Del Toro Cano, F., 539 (Lep.)
 Demanez, M. L., 863 (Lep.)
 Demidowa, A. J., with Bogojawlenski & Melikowa, 482 (K.A.)
 Demidowa, L. W., with Kritschewski, 410 (Mal.)
 Dempsey, J. G., with Thompson & Toombs, 148 (Mal.)
 Denecke, K. & Malamos, B., 423 (Mal.)
 Denney, O. E., 331, 338 (Lep.)
 Deprat, 455 (Pl.)
 Dérôt, M., with Rathery & Conte, (493) (K.A.)
 Deschies, R., 192 *ter*, 778 (Am.)
 Des Essarts, J. Q. & Lefrou, G., 339 (Lep.)
 —, with —, 861 (Lep.)
 Desnos, E. H., 877 (Y.F.)
 —, with Stefanopoulo & Mollaret, 290 (Y.F.)
 Deutsch, B., 832 (Bl.)
 Devasagayam, A., (532) (Misc.)
 Dhont, C. M., Schüffner, W. A. P. & Snijders, E. P., 288 (Y.F.)
 Dias, E., 363, 365, 722 (S.S.)
 —, with Vilella, 366 *bis* (S.S.)
 Dinger, J. E., 165 (Fev.)
 Diniz, O., 856 (Lep.)
 Dios, R. L., with Fülleborn & Zuccarini, 637 *bis* (Hel.)
 —, de Sommerville, E. T. W., Bonacci, H., Aldao, A. & Barba, R., 511 (Misc.)
 Dirckze, H. A., with Sweet, 269 (Hel.)
 Disini, D., with Lagrosa & Tiong, 868 (Lep.)
 Dixon, H. B. F. & Smithers, D. W., 631 (Hel.)
 Djaparidse, P. S., 743 (Mal.)
 Do Amaral, A., Apantes, J. B. & da Fonseca, F., 217 (Misc.), 383 (Sn.)
 Dobell, C., 658 (Misc.)
 Dobradin, P. M. & Skorodumov, A., 451 (Pl.)
 Dobref, M., 216 (Misc.)
 Dodd, K. & Tompkins, E. H., 219 (Misc.)
 Dogra, J. R., (146) (Mal.)
 Donatelli, L., (532) (Misc.)
 Donatien, A. & Lestoquard, F., 491 (K.A.)
 —, with Parrot, 484 (K.A.)
 Doorenbos, W., 457, 763 (Chl.)
 Dopff, C. S. & Conforto, A. V., (170) (Fev.)
 Dorolle, Chaussinard, R. & Tran-van-Tam, 608 (Rab.)
 Dorolle, P. & Ngo-Quang-Ly, 545, (554) (Lep.)
 —, — & Tran-van-Tam, 346 (Lep.)
 Dostrovsky, A., 89 (K.A.)
 Dove, W. E. & Hall, D. G., 662 (Misc.)
 Draganesco, S., with Marinesco, 179, 617 (Rab.)
 Dragomir, L., with Urechia, (675) (Misc.)
 Drensky, K. & Collins, R. K., 106 (Mal.)
 Dreosti, A. O., 494 (H.S.)
 Dreyfus, M., (915) (Misc.)
 Dreyfuss, A., 507 (Misc.)
 van Driel, B. M., 508 (Misc.)
 Drinker, C. K., with Homans & Field, 273 (Hel.)
 Dubois, A. & Degotte, J., 341 (Lep.)
 —, Westerlinck, H. & Degotte, J., 546, 870, 873 (Lep.)
 Dudley, S. F., 283 (Y.F.)
 Duke, H. L., 8, 10, 31, 32, 688, 690, 691, 708 (S.S.), 785 (Mal.)
 —, Mettam, R. W. M. & Wallace, J. M., 33 (S.S.)
 Dumont, R., 687 (S.S.)
 Dunn, E. E., 377 *bis* (Sn.)
 Dunn, L. H., 38 *bis* (S.S.), (674), 667 (Misc.), 806 (Mal.)
 Dünner, L., Hirschfeld, H. & Gerald, M., (49) (Sp.)
 Dupoux, R., with Villain & Marini, 805 (Mal.)
 Duprat, (853) (Pl.)
 Dupuy, 682 (S.S.)
 Durand, R., 164 *bis* (Fev.)
 — & Hombourger, K., 565 (Fev.)
 —, with Laigret, 164 (Fev.), 571 (Fev.)
 Duren, A., 288 (Y.F.)
 —, with Mouchet, van Hoof, Fornara Clarebout, Henry & Henrard, 280 (Y.F.)
 — & van den Branden, F., 349 (S.S.)
 Durieux, C., with Mathis & Advier, 288 (Y.F.)
 —, with — & Laigret, 284 (Y.F.)
 du Toit, R. M., with Nieschulz, 663 (Misc.)
 Dutt, A., with Chopra & Ghosh, (532) (Misc.)
 Dutta, N. C., (554) (Lep.)
 Duval, C. W., (198) (Am.), 550 (Lep.)
 Duvoir, M. E., with Brumpt & Sainton, (279) (Hel.)
 Duwez, J., with van Nitsen, 305 (B.R.)
 Dyer, R. E., 160 (Fev.)
 Dyke, H. W., 539 (Lep.)

E

- Earle, W. C., with Howard & Muench, 739 (Mal.)
 Earnshaw, P. A., (198) (Am.)
 Eaton, L. S., with Russell, 144 (Mal.)
 Eaton, P., 423 (Mal.)
 Economic Advisory Council, 677 (S.S.)
 Edwards, J. T., 821 (Bl.)
 Egypt, 233 (Hel.)
 Egypt, Ministry of the Interior, 900 (Misc.)
 Egyptian Government, 397 (Mal.)
 Eichholtz, F., 747 (Mal.)
 — & Erhardt, A., 252 (Hel.)
 Eilmann, H., 269 (Hel.)
 Eisbach, L., 246 (Hel.)
 Ejercito, A., 98, 816 (Mal.)
 Ekblom, T., 812 (Mal.)
 El Diwany, M. A. El M., 247 (Hel.)
 Elliot, R. H., 898 (Oph.)
 Ellis, M., 16 (S.S.)

Elmes, B. G. T., with Smith, 523 (Misc.)
 Emara, 621 (Hel.)
 Emerson, G. A., 343 (Lep.)
 — & Anderson, H. H., 347, 548 (Lep.)
 —, — & Leake, C. D., 549 (Lep.)
 Engelbreth-Holm, J., with Lomholt, 866 (Lep.)
 Enikolopov, S. K., with Chaikin, 734 (Mal.)
 Epstein, E., with Tareev, Bolotina, Gontaeva, & Raskin, 111 (Mal.)
 Epstein, H. & Silvers, I. L., 158 (Fev.)
 —, Turewitsch, E. I. & Exemplarskaja, E. W., 161 (Fev.)
 Erhardt, A., 252 (Hel.)
 —, with Eichholtz, 252 (Hel.)
 Escalar, G., with Pecori, 404 (Mal.)
 Eskey, C. R., 446 (Pl.)
 Eskin, V. A., with Lisova, 724 (Mal.)
 Eskridge, L., with Hegner, 659 *bis* (Misc.)
 Esmenard, J., with Joyeux & Sédan, 899 (Oph.)
 Esposito, G., 774 (Am.)
 Estrade, F., 846 (Pl.)
 —, with Girard, 454 (Pl.)
 Eva, A., with Clunie, 519 (Misc.)
 Evans, A. C., 666 (Misc.)
 Evans, A. M., 438 (Mal.)
 — & Leeson, H. S., 804 (Mal.)
 Exemplarskaja, E. W., with Epstein & Turewitsch, 161 (Fev.)

F

Faccioli, D., 815 (Mal.)
 Façon, E., with Marinesco, 617 (Rab.)
 Fairley, N. H., 373 (Sn.)
 — & Bromfield, R. J., 210 *bis*, 828 (Bl.)
 —, with Low, 45 (Sp.)
 —, with Mackie, 46 (Sp.)
 Fakhry, A., 236 *bis* (Hel.)
 Fan, P. L. & Scott, A. V., 483 (K.A.)
 Far Eastern Association of Tropical Medicine, 761 (Chl.), 758 (B.R.), 841 (Pl.)
 Faria, A., with Braga, 608 (Rab.)
 Farinaud, E., 143 *bis* (Mal.)
 Farinaud, M. E., 786 (Mal.)
 Farmakadis, C., (781) (Am.)
 Fast, J., 508 (Misc.)
 Faure-Brac, with Augier, 490 (K.A.)
 Faust, E. C., (198) (Am.)
 —, with Hinman & DeBakey, 277 (Hel.)
 — & Hoffman, W. A., 245 (Hel.)
 —, —, Jones, C. A. & Janer, J. L., 244 (Hel.)
 —, Jones, C. A. & Hoffman, W. A., 625 (Hel.)
 — & Kagy, E. S., 190, 191 (Am.)
 —, with Riley & Griffiths, 106 (Mal.)
 —, Scott, L. C. & Swartzwelder, J. C., 777 (Am.)
 —, Wells, J. W., Adams, C. & Beach, T. D., 267 (Hel.)
 Faz Tabfo, H., 257 (Hel.)
 Federated Malay States, 138 (Mal.)
 Feemster, R. F., 193 (Dys.)
 Fejjoó, E. J. C., with Raimondi, 36 (S.S.)
 Feng, C. T. & Cheng, C. L., (554) (Lep.)
 Feng, H. H., 255 (Hel.), 475 (Oph.)

Feng, L., 647 (Hel.), 802 (Mal.)
 Fermoselle Bacardi, J., with Kouri & Basnuevo, 628 (Hel.)
 Fernandez, J. M. M. & Schujman, S., 869 (Lep.)
 Fernando, S. E., 274 (Hel.), 475 (Oph.)
 Féron, J., 545 (Lep.)
 Ferreira, B. G., (444) (Mal.)
 Ferreira, J. C., 795 (Mal.)
 Ferris, G. F., 913 (Misc.)
 Ficacci, L., (752) (Mal.)
 Field, J. W., 114 (Mal.)
 — & Kandiah, M., 416 (Mal.)
 Field, M., with Homans & Drinker, 273 (Hel.)
 Fiessinger, N., 492 (K.A.)
 Fillion, H. & Millischer, P., 658 (Misc.)
 Findlay, G. M., 285, 286 (Y.F.)
 — & Brown, H. C., 120 (Mal.)
 — & Clarke, L. P., 289, 290, 590 (Y.F.)
 —, Hower, T. F. & Clarke, L. P., 291 (Y.F.)
 — & Stern, R. O., 593 (Y.F.)
 Fine, J., 36 (S.S.)
 Fiol, H., with Puente, (555) (Lep.)
 Fiorentino, A., with Paradiso, 534 (B.R.)
 Fischer, F. P. & Fischl, V., 222 (Misc.)
 Fischer, O., (781) (Am.)
 Fischl, V., 702 (S.S.)
 —, with Fischer, 222 (Misc.)
 — & Fischl, L., 358 (S.S.)
 — & Singer, E., 355, 701, 708 (S.S.)
 —, with —, 355, 703 (S.S.)
 —, with — & Kotrba, 24 (S.S.)
 Fisher, A. C., 239, 247 (Hel.)
 Fisk, R. T., with Hoyt & Thienes, 618 (Rab.)
 Fitte, O. E., 721 (S.S.)
 Fitzgerald, G. H. & Gupta, P. K. D., 55 (Y. & S.)
 Fivoli, F., 58 (Y. & S.)
 Fletcher, W., 410 (Mal.)
 Flinker, R., (470) (Pel.)
 Flu, P. C., (853) (Pl.)
 —, with Hulshoff, (674) (Misc.)
 Foley, H. & Parrot, L., 397 (Mal.)
 Fons Diaz, O., (146) (Mal.)
 da Fonseca, F., with Do Amaral & Arantes, 217 (Misc.)
 —, with — & Arantes, 383 (Sn.)
 Forkner, C. E. & Zia, L. S., 479 (K.A.)
 —, with —, 482, 483 (K.A.)
 Fornara, L., with Mouchet, van Hoof, Duren, Clarebout, Henry & Henard, 280 (Y.F.)
 Fort, M. A., (146) (Mal.)
 Foster, A. O. & Cort, W. W., 641 (Hel.)
 — & Cross, S. X., 265 (Hel.)
 — & Landsberg, J. W., 259 (Hel.)
 Foster, J. W., with Spector & Glover, (773) (Am.)
 Fourest, with Gimbert, Andreoli & Housiaux, 168 (Fev.)
 Fox, H., 90 (K.A.)
 — & Knott, J., 545 (Lep.)
 Fradkin, W. Z., (198) (Am.)
 Francke, M., with Slatineanu, Balteanu, Sibi, Nitzulescu, Cantacuzino, Paraschivescu, Veit & Lupu, 469 (Pel.)
 —, with Slatineanu, Ciuca, Balteanu, Alexa, E., Alexa, I. & Rugina, 411 (Mal.)
 Franco, E. E., 480 (K.A.)

- Franco, J. J. & Colichón, H., 600 (R.B.F.)
 Francois, J., 471 (Oph.)
 Franke, M., with Ciuca & Alexa & Agapi, C.,
 Pupu, E. & Manoliu, 745 (Mal.)
 Fraser, N. D., 872 (Lep.)
 Frawley, J. M. & Ginsburg, H. M., 915
 (Misc.)
 —, with —, 915 (Misc.)
 Freeman, A. R. & Torres, A. N., 146 (Mal.)
 Freeman, M. & Kellaway, C. H., 374 (Sn.)
 —, with Williams & Kennedy, 374 (Sn.)
 Freund, H. A., 198 (Am.)
 Freund, L., 256 (Hel.)
 Freville, L. H. F., 345, 547 (Lep.)
 Frey, S., 382 (Sn.)
 Fróes, H. P., (147), 423 (Mal.), 482 (K.A.),
 671 (Misc.), 603 (B.R.)
 Frohn, W., 584 (Fev.)
 Frugoni, C., (582) (Fev.)
 Frye, W. W. & Meleney, H. E., 779 (Am.)
 —, with —, 180, 779 (Am.)
 Fujibayashi, M., 361 (S.S.)
 —, with Komiya, (43) (S.S.)
 Fülleborn, F., Dios, R. L. & Zuccarini, J. A.,
 637 *bis* (Hel.)
 Funayama, J. I., 177 *bis* (Rab.)
 Funk, W. H., (170) (Fev.)
- G**
- Gaafar, M., with Azmy & Noshokati, 527 *bis*
 (Misc.)
 Gaignaire, 743 (Mal.)
 Galavieille, R., with d'Oelsnitz & Raybaut,
 (493) (K.A.)
 Galinier, G., 56 (Y. & S.)
 Gallardo, V. P., (279) (Hel.)
 Galliard, H., 42 (S.S.), 813 (Mal.)
 —, with Brumpt, 486 (K.A.)
 — & Sautet, J., 403, (445) (Mal.)
 Galli-Valerio, 382 (Sn.)
 Galt, C. M. & Yawt, N., 334 (Lep.)
 Gambrell, E., with Huff, 119 (Mal.)
 Ganguli, S. K., with Chopra, 788 (Mal.)
 —, with — & Roy, 787 (Mal.)
 —, with — & Sen, 113 (Mal.)
 Gan Sing Bie, with Soetjahjo, 3 (Bb.)
 Garcia, E. Y., with Africa, 776 (Am.)
 García Robin, A., with Patiño Mayer, (782)
 (Am.)
 Gardiner, M. L., with Miller, 255 (Hel.)
 Gardner, A. D. & Venkatraman, K. V., 461,
 769 (Chl.)
 Gaschen, 133 (Mal.)
 Gaschen, H., 403, 801, 802 *bis* (Mal.)
 Gaud, M., with Blanc, 570 (Fev.)
 Gauthier, H., 243 (Hel.)
 Gautier, C. & Bissery, 600 (R.B.F.)
 Gautrelet, J. & Halpern, N., 378 (Sn.)
 —, — & Corteggiani, E., 379 (Sn.)
 Gay, M. A. P., with Varela, 160 (Fev.)
 —, with — & Aguayo, 564 (Fev.)
 Geay, M., 902 (Misc.)
 Gelfand, B. B., with Appelbaum, 108 (Mal.)
 Gentilucci, A. S., 608 (Rab.)
 Geoghegan, A. J., (370) *bis* (S.S.)
 Geracitano, A., with Castronuovo, 422 (Mal.)
- Gerald, M., with Dünner & Hirschfeld, (40)
 (Sp.)
 Ghose, A. K., 216 (Misc.)
 Ghosh, B. M., 832 (Bl.)
 Ghosh, B. N., 918 (B.R.)
 — & Nath, M. C., 422 (Mal.)
 —, with Sinton, 127 (Mal.)
 —, with Wats, 749 (Mal.)
 Ghosh, H., 459 (Chl.)
 Ghosh, L. M., with Acton, 184 (Der.)
 Ghosh, S., with Chopra, 528 (Misc.)
 —, with — & Dutt, (532) (Misc.)
 Gibson, D., with Strickland, 140 (Mal.)
 Giglioli, G., 214 (Bl.)
 Gilbert, E. W. & Stewart, C. M., 673 (Misc.)
 Gil Collado, J., with Cartaña Castilla, 307
 (B.R.)
 Gilks, J. L., 83 (K.A.)
 Gill, D. G., with Baker & McAlpine, 564 *bis*
 (Fev.)
 Gillan, R. U., 71 (Misc.)
 Gille, R., with Benhamou, 791, 793 (Mal.)
 Gillier, M. R., 552 (Lep.)
 Gillier, R., 340 (Lep.)
 Gilmour, C. C. B., 450 (Pl.)
 Gimbert, Andreoli, Houssiaux & Fourest, 168
 (Fev.)
 Ginandes, G. J., 493 (K.A.)
 Ginsburg, H. M., with Frawley, 915 (Misc.)
 Giordano, A., 534 (B.R.)
 Giordano, M., 191 (Am.), 520 (Misc.), 575
 (Fev.)
 Giovannola, A., 122, 128, (445), 737 (Mal.)
 Girard & Paulevich, 600 (R.B.F.)
 Girard, G., 452, 850 (Pl.)
 — & Estrade, F., 454 (Pl.)
 — & Robic, J., (456) (Pl.)
 Giraud, P., 480, 482, 484 *bis* (K.A.)
 — & Ciaudo, P., 88 (K.A.)
 — & Poursines, Y., 84 (K.A.)
 — & Vigne, P., 84 (K.A.)
 Girges, R., 257 *bis*, (279), 636 (Hel.)
 Giroud, P. & Haber, P., 568 (Fev.)
 —, with Nicolle, 557, 558 *bis*, 559, (582)
 (Fev.)
 Giunta, G., (834) (Bl.)
 Glover, N. G., with Spector & Foster, (773)
 (Am.)
 Gnedina, M., with Podyapolskaya, 232 (Hel.)
 Gnezdilov, V., 780 (Am.)
 Gobert, E., 243 (Hel.), 846 (Pl.)
 —, with Anderson, 243 (Hel.)
 Godbole, G. B., with Vengsarkar & Raghavan,
 228 (Misc.)
 Godinho, R., with Prado, (753) (Mal.)
 Gohar, M. A., 851 (Pl.)
 Goinard, P., with Catanei, 182 (Der.)
 Goldblatt, I., 825 (Bl.)
 Goldie, H., 355 (S.S.)
 Goldwater, L. J., with Curran & Connery,
 (874) (Misc.)
 Golob, M., 634 (Hel.)
 Goltman, D. W., with Mitchell, (753) (Mal.)
 Gomes, J. M., 331 (Lep.)
 Gomez, B., with De la Plaza & Vegas, 871
 (Lep.)
 Gomez, J. M., 341 (Lep.)
 Gontaeva, A., with Tareev, Bolotina, Raskin
 & Epstein, 111 (Mal.)

- Gonzaga, A. G. & Leão, A. E. A., 182 (Der.)
 Gonzales, H. D., 180 (Rab.)
 González, J. O., with Bachman & Molina, 268 (Hel.)
 Gorchowa, E. L., with Sinelnikow, Moldaws-kaja-Kritschewskaja, Althausen & Gritzay, 792 (Mal.)
 Gordon, R. M., 295 (Y.F.)
 —, Davey, T. H. & Peaston, H., 237 (Hel.)
 Gorgas Memorial Institute, (532) (Misc.)
 Gouget, R., 99 (Mal.)
 Gourry, N., with Riou & Hussenet, 112 (Mal.)
 Gourvil, E., 538 (Lep.), 589 *bis* (Y.F.)
 Gow, W. H., 473 (Oph.)
 Grace, A. W., 271 (Hel.)
 Graham, G. L., 269 (Hel.)
 Grall, G., (724) (S.S.), 881 (Y.F.)
 Grams, H., 658 (Misc.)
 Grant, A. M. B., 330 (Lep.)
 Grasset, E., with Pirie, 852 (Pl.)
 Grau, C. A., with Beretervide, 776 (Am.)
 Grayson, C. T., Martin, F. & Clark, H. C., (532) (Misc.)
 Grayson, W. B., (147) (Mal.)
 Greco, Z., 91 *bis* (K.A.)
 de Greef, R., (227) (Misc.)
 Green, H., with Nadler & Rosenbaum, 216 (Misc.)
 Green, R., 391 (Mal.)
 Greenfield, G., 734, (752) (Mal.)
 Greenway, D., with Castex, (198) *bis* (Am.)
 Greig, E. D. W., Hendry, E. B. & van Rooyen, C. E., 131 (Mal.)
 —, van Rooyen, C. E. & Hendry, E. B., 129 *ter* (Mal.)
 Greval, S. D. S., 384 (Sn.)
 Griffith, G., 661 (Misc.)
 Griffiths, T. H. D., 106 (Mal.)
 —, with Hanson & Boyd, 735 (Mal.)
 —, with Riley & Faust, 106 (Mal.)
 Grigaut, A., with Marchal & Soulié, (279) (Hel.)
 Grigorowski, A. M., with Kritschewski, Magidson & Halperin, 419 (Mal.)
 Grikurov, W., 450 (Pl.)
 Grillo, J. & Krumeich, R., 298 (R.F.)
 Grimard, L., with Nattan-Larrier, 485 (K.A.)
 Grimard-Richard, L., with Nattan-Larrier, 85 *ter*, 87, 484 (K.A.)
 —, with — & Nougues, 85 (K.A.)
 Grimes, C., Cluzet & Minec, 869 (Lep.)
 Grinberg, A., with Tudoranu & Herescu, 128 (Mal.)
 Gritzay, A. A., with Sinelnikow, Moldaws-kaja-Kritschewskaja, Gorchowa & Althausen, 792 (Mal.)
 Grizaud, H., 171 (Fev.)
 de Groat, A., with Thompson, (873) (Lep.)
 Gross, M., 197 (Dys.)
 Grossmann, J., with Jelin & Linetzskaja, 161 (Fev.)
 Gruber, G. B., (655) (Hel.)
 Guardabassi, M., 609 (Rab.)
 Guccione, F., (147) (Mal.)
 Guerrieri, T., (348) (Lep.)
 Guerrini, F. Z., with Mazza, 36 (S.S.)
 Guillerm, J., Banos, M. & Nguyen-Van-Lien, 342 (Lep.)
 Gulbransen, R., with Browning, 28, 705, 706 (S.S.)
 —, with — & Cappell, 30 (S.S.)
 Gupta, B. M. D., 221 (Misc.)
 —, with Chopra & Roy, 412 (Mal.)
 —, with Knowles, 222 (Misc.), 799 (Mal.)
 Gupta, P. K. D., with Fitzgerald, 55 (Y. & S.)
 Gutierrez-Solano, with Solana (873) (Lep.)
 Guy, R., (445) *bis* (Mal.), 620 (Hel.)
 —, with Monier & Ros, 401 (Mal.)
 Guzewiç, A. W., 906 (Misc.)
 Guzewitsch, A. W. & Podoljan, W. J., (915) (Misc.)
- H
- Haber, P., with Giroud, 568 (Fev.)
 Hackett, C. J., 891 (Y. & S.)
 Hackett, L. W., 138 (Mal.)
 — & Missiroli, A., 809 *bis* (Mal.)
 Hall, D. G., with Dove, 662 (Misc.)
 Hall, G. R., 202 (Bl.)
 Hall, M. C., 233 (Hel.)
 Haller, H. L., with Campbell, Sullivan & Smith, 663 (Misc.)
 Hallinan, T. J., 637 (Hel.)
 Halperin, E. P., with Kritschewski, Magidson & Grigorowski, 419 (Mal.)
 Halpern, N., with Gautrelet, 378 (Sn.)
 —, with — & Corteggiani, 379 (Sn.)
 Hamel, J. & Chavarot, M., (445) (Mal.)
 Hancock, G. L. R., 661 (Misc.)
 Handler, B. J., 360 (S.S.)
 Hanifah, A., (834) (Bl.)
 Hanson, H., (147) (Mal.)
 —, Boyd, M. F. & Griffiths, T. H. D., 735 (Mal.)
 Happold, F. C., with Boxhall & Lloyd, 222 (Misc.)
 Harbhagwan, with Chand, 800 (Mal.)
 Hargrove, M. D., (781) (Am.)
 Harrower, G., 862 (Lep.)
 Harwood, P. D., 237 (Hel.)
 —, with Lamson & Brown, 237 (Hel.)
 —, with Melaney, 668 (Misc.)
 Hasle, G., with Vaucel, 566 (Fev.)
 Hassan, A. & Betashe, M., 250 (Hel.)
 — & Salah, M., 621 (Hel.)
 —, with —, 248 (Hel.)
 Hasselmann, C. M., 185 (Der.), 205 (Bl.), 893 (Y. & S.)
 Hassko, A., 706 *bis* (S.S.)
 Hauer, A., (752) (Mal.)
 Hauser, W., 498 (C.Bu.)
 Hautefeuille, J., (279) (Hel.)
 Hayashi, F., 334 (Lep.)
 Hayashi, N., Matsuoka, S., Kato, T. & Okamoto, N., 169 (Fev.)
 Hayes, G. H., 185 (Der.)
 Haythornthwaite, R. A., with Morison & Rice, 460 (Chl.)
 Hecht, G., 747 (Mal.)
 Hegler, C. & Nauck, E. G., 77 (B.R.)
 Hegner, R., 220, 223, 224 (Misc.), (781) (Am.)
 — & Eskridge, L., 659 *bis* (Misc.)
 Helfferich, W. M. G., 96 (Mal.)
 Helman, J., 564 (Fev.)

- Helpern, M., 405 (Mal.)
 Hemenway, R. V., (198) (Am.)
 Hemming, F., 677 (S.S.)
 Henderson, L. H., 143 (Mal.)
 Hendry, E. B., with Greig & van Rooyen, 129 *ter*, 131 (Mal.)
 Hennessey, R. S. F., 156 (Fev.)
 Henrard, C., 369 (S.S.)
 —, with Mouchet, van Hoof, Duren, Fornara, Clarebout & Henry, 280 (Y.F.)
 —, with Vincke, 100 (Mal.)
 Henry, A. F. X., 132, (445), (752), 790 (Mal.)
 Henry, E., with Mouchet, van Hoof, Duren, Fornara, Clarebout & Henrard, 280 (Y.F.)
 Henry, X., 132 (Mal.)
 Henry Lester Institute of Medical Research, 65 (Misc.)
 Herbert, H., 896 (Oph.)
 Herescu, D., with Tudoranu & Grinberg, 128 (Mal.)
 Herms, W. B., (674) (Misc.)
 —, Bailey, S. F. & McIvor, B., 914 (Misc.)
 Hertig, A. T., 226 (Misc.)
 Hesterlow, A. M. V., 453 (Pl.)
 Hetsch, H., with Kolle, 75, 307 (B.R.)
 Hewer, T. F., 53 (Y. & S.)
 —, with Findlay & Clarke, 291 (Y.F.)
 Hicks, E. P. & Chand, D., 749 (Mal.)
 Hill, R. B., 439 (Mal.)
 — & Olavarria, J., (147) *bis* (Mal.)
 —, with —, 815 (Mal.)
 —, — & Rivera, J., 814 (Mal.)
 —, with Rivera, 814 (Mal.)
 Hilmy, I. S., 621 (Hel.)
 Hingst, H. E., 109 (Mal.)
 Hinman, E. H., 106 (Mal.)
 —, Faust, E. C. & DeBakey, M. E., 277 (Hel.)
 — & Kampmeier, R. H., 671 (Misc.)
 Hinshaw, H. C. & Showers, E. M., 188 (Am.)
 Hirano, N., 174 (Rab.)
 Hirayama, S., 187 (Am.)
 Hirschfeld, H., with Dünner & Gerald, (49) (Sp.)
 Hisamochi, Y., 865 (Lep.)
 Hiyeda, K., 509, 903 (Misc.)
 Hoang-Pho, 535 (Lep.)
 Hoare, W. W., 471 (Oph.)
 Hoffman, W. A., with Faust, 245 (Hel.)
 —, with — & Jones, 625 (Hel.)
 —, with —, — & Janer, 244 (Hel.)
 Hoffmann, C. C., 101, 816 (Mal.)
 Hoffmann, J. M., Mertens, W. K. & Snijders, E. P., 171 (Fev.)
 Hoffmann, W. H., (595), (882) (Y.F.), 789 (Mal.), 859 (Lep.)
 — & Baez, P. R., 551 (Lep.)
 — & Ramos Baez, P., (555) (Lep.)
 Hogue, M. J., 191 (Am.)
 Holden, H. F., 380 (Sn.)
 Hollenbeck, H. S., 538 (Lep.)
 Homans, J., Drinker, C. K. & Field, M., 273 (Hel.)
 Hombourger, K., with Durand, 565 (Fev.)
 Honess, R. F., with Owen & Simon, 188 (Am.)
 van Hoof, L., 503 (Misc.)
 —, with Mouchet, Duren, Fornara, Clarebout, Henry & Henrard, 280 (Y.F.)
 Hoops, A. L., 726 (Mal.)
 Hopkins, H. O., 110 (Mal.)
 Hoskins, M., 294 (Y.F.)
 Houdemer, E., with Phisalix, 372 (Sn.)
 Houssiaux, with Gimbert, Andreoli & Fourest, 168 (Fev.)
 Houwer, A. W. M. & Mingelen, R., 898 (Oph.)
 Hoverson, E. T. & Petersen, W. F., 217 (Misc.)
 Howard, H. H., Earle, W. C. & Muench, H., 739 (Mal.)
 Hoyt, A., Fisk, R. T. & Thienes, C. H., 618 (Rab.)
 Hsu, S. C., with Yao & Ling, 619 *bis* (Hel.)
 Hu, S., with Toumanoff, 437 (Mal.)
 Hu, S. M. K., 270, 647 (Hel.)
 —, with Robertson, 99 (Mal.)
 — & Yen, C. H., 646 (Hel.)
 Huang, K. K., with Yang, 466 (Pel.)
 Huard, P. & Renucci, N., 524 (Misc.)
 Hudson, E. H., 891 (Y. & S.)
 Huff, C. G. & Gambrell, E., 119 (Mal.)
 Hughes, T. P., 293 (Y.F.)
 —, with Bauer, 593 (Y.F.)
 —, with Theller, 590 (Y.F.)
 Huizenga, L. S., 535, (555), 858 (Lep.)
 Hulshoff, A. A., 626 (Hel.)
 — & Flu, P. C., (674) (Misc.)
 Hulst, L. A., with Brester, (470) (Pel.)
 Hurst, E. W., 175 (Rab.)
 Hussein, A. G., (456) (Pl.)
 Hussenet, S., with Riou & Gourry, 112 (Mal.)
- I
- Ichihara, T., 864 (Lep.)
 Iglesias, D., 88 (K.A.)
 Ignacio, J., with Lagrosa, 868 (Lep.)
 Ikeda, K., (781) (Am.)
 Ilvento, 102 (Mal.)
 Imagawa, Y., with Kawamura & Ito, 578 (Fev.)
 Impallomeni, R., (674) (Misc.)
 International Convention for Mutual Protection against Dengue Fever, Athens, (172) (Fev.)
 Ioff, I. G., 463 (B.R.)
 — & Argyropulo, A., (674) (Misc.)
 Irgang, S. & Alexander, E. R., 520 (Misc.)
 Ishibashi, T., with Ota, 551 (Lep.)
 —, with — & Sato, (555) (Lep.)
 Ishioka, H., with Morishita & Miyahara, 745 *bis* (Mal.)
 Ishizu, S., with Tōyama, 544 (Lep.)
 Iskandar, F., 773 (Am.)
 Ismail, A., 785 (Mal.)
 Israël, L., with Merklen, 492 (K.A.)
 Issa, I. I., with Ashkar, (655) (Hel.)
 Issajev, L. M., 653 *ter* (Hel.)
 Itakura, T., 542, 863 (Lep.)
 Ito, T., with Kawamura & Imagawa, 578 (Fev.)
 Ivanić, M., 794 (Mal.)
 Ivanitski, S., with Schultz, 646 (Hel.)
 Ivy, A. C., with Reid, Anderson & Stubblefield, 194 (Dys.)
 Iyengar, K. R. K., with Sankaran & Beer, 174 (Rab.)
 Iyengar, M. O. T., 738 (Mal.), 844 (Pl.)

J

- Jackson, C. H. N., 368 (S.S.)
 Jackson, R. B., 726 (Mal.)
 Jacono, I., 724 (S.S.)
 —, with Castellani, 181 (Der.)
 Jamaica, 637 (Hel.), 885 (Y. & S.)
 Jame, L. & Aujaleu, E., 557 (Fev.)
 James, C., 526 (Misc.)
 James, J. F., 818 (Mal.)
 James, S. P., 110, 127 (Mal.), 280, 874 (Y.F.)
 —, Nicol, W. D. & Shute, P. G., 737 (Mal.)
 Jamesson, (198) (Am.)
 Jamison, R., 539 (Lep.)
 Jamot, E., 684 (S.S.)
 Jana, A. P., (445) (Mal.)
 v. Jancsó, N. & v. Jancsó, H., 22, 358, 702, 703, 704 (S.S.)
 — & Novák, E., 596 (R.F.)
 Janer, J. L., with Faust, Hofiman & Jones, 244 (Hel.)
 Janisch, E., 669 (Misc.)
 Jan-Kerguistel, A., 847 (Pl.)
 Jansen, J., 175 (Rab.)
 Jatsenko, F., 145 (Mal.)
 Jazimirska-Krontowska, M. C., with Kron-towsky, Savitska & Soliterman, 569 (Fev.)
 Jelin, W., Linetzka, A. & Grossmann, J., 161 (Fev.)
 Jerace, F., (147), 426 (Mal.)
 Jesioran, R., 171 (Fev.)
 de Jesus, P. I., with de Leon & Ramos, (532) (Misc.)
 Jimenez Rivero, M., 858 (Lep.)
 Jobling, B., 911 (Misc.)
 Jofe, H., 205 (Bl.)
 Johnston, H. M., with Turner & Saunders, 50 (Y. & S.)
 Johnston, H. M., Jr., 887 (Y. & S.)
 Jones, C. A., with Faust & Hoffman, 625 (Hel.)
 —, with —, — & Janer, 244 (Hel.)
 Jonesco, D., 610 (Rab.)
 Jonnesco, D., 176 *ter*, 609 (Rab.)
 —, with Proca & Bobes, 180, 618 (Rab.)
 Jordan, P., 339 *bis* (Lep.)
 Jorge, M. E., with Mazza, (43) (S.S.)
 Jorge, R., 280 (Y.F.), 844, (853), (Pl.), 874 (Y.F.)
 Joukov, N., Krassikova, V. & Rylovnikova, T., 114 (Mal.)
 Jourdan, 897 (Oph.)
 Journal of the Indian Medical Association, 6 (Bb.)
 Journal of the Royal Army Medical Corps, 556 (Fev.), 631 (Hel.)
 Journal of the Royal Naval Medical Service, 294 (Y.F.)
 Joyeux, C., Sédan, J. & Esmenard, J., 899 (Oph.)
 Jung Sun, C., with Yao, 726 (Mal.)

K

- Kagy, E. S., with Faust, 190, 191 (Am.)
 Kalabuchov, N., 849 (Pl.)
 Kambayashi, T., 184 (Der.)

- Kamimura, T., 636 (Hel.)
 Kampmeier, R. H., with Hinman, 671 (Misc.)
 Kan, Y., 187 (Am.)
 Kandiah, M., with Field, 416 (Mal.)
 Kang, T. I. & Wilson, R. M., 540 (Lep.)
 Kao, Z. M., with Ku, 619 (Hel.)
 Karve, J. V. & Sundararajan, E. R., 844 (Pl.)
 Kasahara, S., Yoshida, S. & Okamoto, Y., 566 (Fev.)
 Kato, T., with Hayashi, Matsuoka & Okamoto, 169 (Fev.)
 Kauntze, W. H., 844 (Pl.)
 Kawai, T., Nagayoshi, Y. & Koo, C., 187 (Am.)
 Kawamura, M., 864 (Lep.)
 Kawamura, R., Imagawa, Y. & Ito, T., 578 (Fev.)
 Kawana, K., with Komiya & Tao, (655) (Hel.)
 Keevill, A. J., 21 (S.S.)
 Keil, E., 869 (Lep.)
 Keilin, D., Tate, P. & Vincent, M., 912 (Misc.)
 Kellaway, C. H., 374 *ter*, 377 (Sn.), 672 (Misc.)
 —, with Freeman, 374 (Sn.)
 Keller, A. E., 258, 646 (Hel.)
 — & Leathers, W. S., 230 (Hel.)
 —, with —, (279) (Hel.)
 Kelley, W. H. & Sydenstricker, V. P., 740 (Mal.)
 Kellogg, W. H., 847, (853) (Pl.)
 Kemp, H. A., Moursund, W. H. & Wright, H. E., 296 (R.F.)
 Kendrick, J. F., 258 (Hel.)
 Kennedy, E., with Williams & Freeman, 374 (Sn.)
 Kennedy, W. P., 528 (Misc.)
 Kerim, M. A., 789 (Mal.)
 Kernkamp, Y., with Occhino, 56 (Y. & S.)
 Khakhaieva, V., with Okouneviski, 662 (Misc.)
 Khalil, M., 81, 89 (K.A.), 247, 624, (655) (Hel.)
 398 (Mal.)
 — & Salah, M., 247 (Hel.)
 Khambatta, K. D., (456) (Pl.)
 Kharitonov, D. E., 815 (Mal.)
 Khaw, O. K., 629, (655) (Hel.)
 Kian, L. P., 576 (Fev.)
 Kikuth, W., 227, (532) (Misc.), (752) (Mal.)
 — & Schönhöfer, F., (147), 420, (752) (Mal.)
 King, E. F., 476 (Oph.)
 Kingsbury, A. N., 417 (Mal.)
 Kipritch, S., with Yatsenko & Paretskaya, 668 (Misc.)
 Kirilow-Drenowsky, A., 746 (Mal.)
 Kirk, J. B., 64 (Misc.)
 Kirk, R., (445) (Mal.)
 Kirschner, L., 452 (Pl.)
 —, with Noosten & Vos, 73 (Misc.)
 Kirwan, E. O'G., 473 (Oph.)
 Kitabatake, E., (532) (Misc.), (781) *bis* (Am.)
 Kitchen, S. F., with Boyd & Stratman-Thomas, 738 (Mal.)
 Kleine, F. K. & Krause, M., 297 (R.F.)
 Kligler, I. J. & Aschner, M., 163, 571 (Fev.)
 — & Comaroff, R., 715 (S.S.)

Kikuchi, A., 565 (Fev.)
 Kinsler, J., with Fox, 545 (Lep.)
 Knowles, R., 75 (B.R.)
 — & Barn, B. C., 368 (Mal.), 515 (Misc.),
 598 (R.F.), 794 (Mal.)
 — & Gupta, B. M. D., 222 (Misc.), 799
 (Mal.)
 Kô, T., 169 (Fev.)
 Kobashi, S., with Nakamura, 339 (Lep.)
 Koechlin, D., with Chorine, 791 (Mal.)
 —, with — & Prudhomme, 130 (Mal.)
 Kofoid, C. A., McNeil, E. & Bonestell, A.,
 222 (Misc.)
 Koh, T. M., with Rose, (656) (Hel.)
 Koidzumi, M., (655) (Hel.)
 Kojima, T., Yamanaka, S. & Kyu, U. F.,
 166 (Fev.)
 Koks, M. T., with van Veen, 5 (Bb.)
 Kolle, W. & Hetsch, H., 75, 307 (B.R.)
 Komiya, S. & Fujibayashi, M., (43) (S.S.)
 Komiya, Y., Kawana, K. & Tao, S., (655)
 (Hel.)
 Komp, W. H. W. & Clark, H. C., 434, 784
 (Mal.)
 Koo, C., with Kawai & Nagayoshi, 187 (Am.)
 Kopaczewski, W., 491 (K.A.)
 Kopcowska, L., 605 (Rab.), 879 (Y.F.)
 —, with Nicolau, 173, 605 (Rab.)
 —, with — & Mathis, 293 (Y.F.)
 Korossios, N. T., with Laignel-Lavastine &
 Würmser, 378 (Sn.)
 —, with Vernes, 378 (Sn.)
 Korovitski, L. & Artemenko, V., 232 (Hel.)
 Kostareva, E., 91 (K.A.)
 Kotrba, J., with Singer & Fischl, 24 (S.S.)
 Kotter, G. F. & van den Berghe, L., 880
 (Y.F.)
 Kouri, P., Basnuevo, J. G. & Arenas, R.,
 628 *bis* (Hel.)
 —, — & Fermoselle Bacardí, J., 628
 (Hel.)
 Kouwenaar, 521 (Misc.)
 Kouwenaar, W., Maasland, J. H. & Wolff,
 J. W., 521, (532 *bis*) (Misc.)
 — & Wolff, J. W., 578, 579 (Fev.)
 —, with —, 579 (Fev.)
 Krainick, H., with Oesterlin, 236 (Hel.)
 Kratner, H. F., (198) (Am.)
 Krassikova, V., with Joukov & Rylovnikova,
 114 (Mal.)
 Krause, M., with Kleine, 297 (R.F.)
 —, with Kunert, 362 (S.S.)
 Krauss, W., (147) (Mal.)
 Krishnan, K. V., 490 (K.A.), 832 (Bl.)
 —, with Smith & Mukerji, 88 (K.A.)
 Krishnaswamy, T. K., with Menon & Anna-
 malai, 789 (Mal.)
 Kritschewski, I. L. & Demidowa, L. W., 410
 (Mal.)
 —, Magidson, O. J., Halperin, E. P. &
 Grigorowski, A. M., 419 (Mal.)
 — & Pines, A. I., (752) (Mal.)
 — & Rubinstein, P. L., 793 (Mal.)
 Krontowsky, A. A., Jazimirsk-Krontowska,
 M. C., Savitska, H. P. & Soliterman, P. L.,
 569 (Fev.)
 Kroó, H., 297 (R.F.)
 Krumeich, R., with Grillo, 298 (R.F.)

Ku, D. Y., (655) (Hel.)
 — & Kao, Z. M., 619 (Hel.)
 Kubo, M., (782) (Am.)
 Kumm, H. W., 885, 886 (Y. & S.)
 —, Turner, T. B. & Peat, A. A., 886
 (Y. & S.)
 Kundu, M. L., (227) (Misc.)
 Kunert, H. & Krause, M., 362 (S.S.)
 —, with Schilling, Schreck & Neumann, 43
bis (S.S.)
 Kutcher, S., 145 (Mal.)
 Kyu, K., 375 (Sn.)
 Kyu, U. F., 166 (Fev.)
 —, with Kojima & Yamanaka, 166 (Fev.)

L

Labernadie, V., 344 (Lep.)
 Lacaux, J., 143 (Mal.)
 Lacour, P. R., 129 (Mal.)
 Lafleur, (894) (Y. & S.)
 Lagrosa, M., Alonso, J. M., Tiong, J. O. &
 Paras, A., 547 (Lep.)
 — & Ignacio, J., 868 (Lep.)
 —, Tiong, J. O. & Disini, D., 868 (Lep.)
 Lai, D. G., 337, 535 (Lep.)
 Laignel-Lavastine, Würmser, L. & Korossios,
 N. T., 378 (Sn.)
 Laigret, J., 285 *bis*, 287, 879 (Y.F.)
 — & Durand, R., 164, 571 (Fev.)
 —, with Mathis & Durieux, 284 (Y.F.)
 —, with Nicolle, 880 (Y.F.)
 Lal, C., with Smith, 83 (K. A.)
 Lamb, A. R., 553 (Lep.)
 Lambert, S. M., 60 (Misc.)
 Lamborn, W. A., 909 (Misc.)
 —, with Thomson, 68 (Misc.)
 Lampe, P. H. J. & de Moor, C. E., 863 (Lep.)
 Lamson, P. D., Brown, H. W. & Harwood,
 P. D., 237 (Hel.)
 —, Molloy, D. M. & Brown, H. W., 635
 (Hel.)
 Landeiro, F., 788 (Mal.)
 Landsberg, J. W. & Cross, S. X., 641 (Hel.)
 —, with Foster, 259 (Hel.)
 Lane, C., 274, 643, 644 (Hel.)
 de Langen, C. D., 260 (Hel.)
 — & Storm, C. J., 418, 726, (753) (Mal.)
 Langeron, M., 898 (Oph.)
 —, with Brumpt, 183 (Der.)
 Langton, E. A. C., 735 (Mal.)
 Lapage, G., 634 (Hel.)
 Lara, C. B. & de Vera B., 544, 862 (Lep.)
 Large, D. T. M., 195 (Dys.)
 — & Sankaran, O. K., 195 (Dys.)
 Lasnet, (147) (Mal.)
 Lassablière, P. & Peycelon, A., 20, 42 (S.S.)
 Latham, D. V., 526 (Misc.)
 Lauda, E., 197 (Dys.)
 Launoy, L., 353, 708 (S.S.)
 — & Ancelot, A., 354 (S.S.)
 — & Prieur, M., 696 (S.S.)
 Laurel, A. G., 98 (Mal.)
 Lawson, H. A., with Rhoads, Castle & Payne,
 263 *bis* (Hel.)

- Leake, C. D., with Emerson & Anderson, 549 (Lep.)
 Leao, A. E. de A., 218 (Misc.)
 Leão, A. E. A., with Gonzaga, 182 (Der.)
 Lease, J. G. & Parsons, H. T., (532) (Misc.)
 Leathers, W. S. & Keller, A. E. (279) (Hel.)
 —, with —, 230 (Hel.)
 Le Chuiton, F. & Bourgain, M., 568 (Fev.)
 Ledentu, G., 14 (S.S.)
 Lee, H. S., 540 (Lep.)
 Lee, Y., 256 (Hel.)
 Leeson, H. S., 804 (Mal.)
 —, with Evans, 804 (Mal.)
 Lefrou, G. & des Essarts, J. Q., 861 (Lep.)
 —, with —, 339 (Lep.)
 Legendre, F., 144, (445) (Mal.)
 Léger, J. P., 449 (Pl.)
 Leggate, J., 346 (Lep.)
 —, Tjong, J. O. & Disini, D., 868 (Lep.)
 Leiper, R. T., 759 (B.R.)
 Leiva, L., 191 (Am.)
 Lemaire & Ribère, 632 *bis* (Hel.)
 Le Moul't & Pirot, 231 *bis* (Hel.)
 Lentjes, L. J. M., 169 (Fev.)
 Lentz, W. J., with Barnes, Metcalfe & Martindale, 179 (Rab.)
 de Leon, W., de Jesus, P. I. & Ramos, J. M., (532) (Misc.)
 Lépine, P., 160, 565 (Fev.)
 — & Bilfinger, F., 161 (Fev.)
 — & Markianos, J., 546 (Lep.)
 Leprosy in India, 856 (Lep.)
 Leprosy Review, 328, 536 *bis*, 854 (Lep.)
 Le Roux, J. J. du P., with Wade, 544 (Lep.)
 Le Sconézec, 54 (Y. & S.)
 Lester, H. M. O., 685 (S.S.)
 Lestoquard, F., with Donatien, 491 (K.A.)
 Levaditi, C., 607 (Rab.)
 — & Levaditi, J., 499 (C.Bu.)
 —, Schoen, R. & Levaditi, J., 173 (Rab.)
 —, Vaisman, A. & Paic, M., 298 (R.F.)
 Levaditi, J., with Levaditi, C. & Schoen, 173 (Rab.)
 Le-van-Phung, with Montel & Massari, 55 (Y. & S.)
 Le-Van-Trien, with Bigot, 345 (Lep.)
 Levine, J. & Marin, R. A., 627 (Hel.)
 Levit, M. S., with Ruibinski, 819 (Mal.)
 Levy, G., with Sézary & Bolgert, 342 (Lep.)
 Lewis, D. J., 41 (S.S.), 134 (Mal.)
 —, with Buxton, 369 (S.S.)
 Lewis, E. A., 367 (S.S.)
 Lewthwaite, R. & Savor, S. R., 577 (Fev.)
 Ley, J., with Baonville & Titeca, 693 (S.S.)
 Lhérisson, C., 62 (Misc.)
 Li, F., 247 (Hel.)
 — & Wu, S., 661 (Misc.)
 Li, T. Y. & Thompson, H. G., 628 (Hel.)
 Liddo, S., 197 (Dys.)
 Lie, H. P., 537 (Lep.)
 Lieurade, L., 19 (S.S.)
 Lièvre, H., 250 (Hel.)
 Lima, Q., 607 (Rab.)
 Lindberg, K., (753) (Mal.)
 Linders, F. J., with Svensson, 220 (Misc.)
 Lindsay, J. W., (915) (Misc.)
 Linetzka, A., with Jelin & Grossmann, 161 (Fev.)
 Ling, L. C., with Yao, 726 (Mal.)
 Ling, S. C., with Yao & Hsu, 619 *bis* (Hel.)
 Linton, R. W., 768, (772) (Chl.)
 — & Mitra, B. N., 461 (Chl.)
 — & Seal, S. C., (772) (Chl.)
 —, Shrivastava, D. L. & Mitra, B. N., (462) (Chl.)
 —, Singh, H. & Seal, S. C., 772 (Chl.)
 Lipatova, T., 454 (Pl.)
 Lisova, A. I. & Eskin, V. A., 734 (Mal.)
 Lister, S., 66 (Misc.)
 Liu, K. B., (753) (Mal.)
 Liu, L. S., (753) (Mal.)
 Lloyd, L., with Boxhall & Happold, 222 (Misc.)
 Lloyd, W. & Mahaffy, A. F., 289 (Y.F.)
 Loewenstein, E., 550, 861 (Lep.)
 Loewenthal, L. J. A., 182, 185 (Der.)
 Logie, H. B., 463 (B.R.)
 Lombardo, F., 576 (Fev.)
 Lomholt, S. & Engelbreth-Holm, J., 866 (Lep.)
 Long, J. D., 848 (Pl.)
 — & Mostajo, B., 448 (Pl.)
 van Loon, J. P., (532) (Misc.)
 López, C., with Steiner, 608 (Rab.)
 Lopez-Neira, C., (279) (Hel.)
 Lopez Neyra, C. R. & Suarez Peregrin, E., 224 (Misc.)
 Lorando, N., 564 (Fev.)
 Lossev, L., 256 (Hel.)
 Lotsong, S., with Tchang, 567 (Fev.)
 Loucks, H. H., 619 (Hel.)
 Lounsbury, C. R., 381 (Sn.)
 Lourie, E. M., 117, 415, 416 (Mal.)
 —, Murgatroyd, F. & Yorke, W., 697 (S.S.)
 Love, J., (147) (Mal.)
 Low, G. C., 278 (Hel.)
 — & Cordiner, G. R. M., 672 (Misc.)
 — & Fairley, N. H., 45 (Sp.)
 — & Manson-Bahr, P. H., 274 (Hel.)
 Lowe, J., 336, 550, (555) (Lep.), 424 (Mal.)
 Lowenthal, H. F. & Roberts, R. A., 244 (Hel.)
 Lutrot, M., 624 (Hel.)
 Lupu, D., with Slatineanu, Balteanu, Sibi, Nitzulescu, Franche, Cantacuzino, Paraschivescu & Veit, 469 (Pel.)
 Lwoff, A., 223 (Misc.)
 Lynch, K. M., (198) (Am.)

M

- Maasland, J. H., with Kouwenaar & Wolff, 521, (532 *bis*) (Misc.)
 McAlpine, J. G., with Baker & Gill, 564 *bis* (Fev.)
 MacCallan, A. F., 471, 896 (Oph.)
 McCarrison, R., Sankaran, G. & Beer, W. A., 174 (Rab.)
 McCay, F. H., (198) (Am.)
 McClean, S. D. & Marsh, F., 194 (Dys.)
 McClosky, A. J., 71 (Misc.)
 McClure, R. B., 82 (K.A.)
 McCoy, G. W. & Chesley, A. J., (198) (Am.)
 McCoy, O. R., 645 (Hel.)
 MacDonald, A. E. & McKenzie, K. G., 899 (Oph.)

- McDonald, W. M., 733 (Mal.)
 Macfarlane, R. G. & Barnett, B., 380 (Sn.)
 —, with —, 381 (Sn.)
 McGuire, J. P., with Shortt, Brooks & Stephens, 610 (Rab.)
 McIvor, B., with Herms & Bailey, 914 (Oph.)
 Mackay, R., (147) (Mal.)
 Mackehenie, D., 583 (Fev.)
 McKendrick, A. C., 616 (Rab.)
 McKenzie, K. G., with Macdonald, 899 (Oph.)
 Mackerras, I. M., 672 (Misc.)
 Mackie, F. P., 350 (S.S.), 821 (Bl.)
 — & Fairley, N. H., 46 (Sp.)
 Mackie, T. T., 44 (Sp.), 513 (Misc.)
 McKinley, E. B., 64 (Misc.), 535 (Lep.)
 MacLeod, J. M. H., 493 (K.A.), 541 (Lep.)
 McMahon, J. P., 910 (Misc.)
 McMillan, J. S., 494 (H.S.)
 McNabb, P. E. & Schwartz, S. C., 111 (Mal.)
 Macnamara, C. V., 572 (Fev.)
 McNeil, E., with Kofoed & Bonestell, 222 (Misc.)
 McRobert, G. R., 72 (Misc.)
 Madras, 247 (Hel.), 453 (Pl.)
 Maegraith, B., 71 (Misc.)
 de Magalhaes, O., (674) (Misc.)
 —, with Moreira, 157 (Fev.)
 Magasin de Parasitologie de l'Institut Zoologique de l'Académie des Sciences de l'URSS, 906 (Misc.)
 Magath, T. B., (199) (Am.), 660 (Misc.)
 Magidson, O. J., with Kritschewski, Halperin & Grigorowski, 419 (Mal.)
 Mahaffy, A. F., with Beeuwkes, Burke & Paul, 282 (Y.F.)
 —, with Lloyd, 289 (Y.F.)
 Majewski, C., 472 (Oph.)
 Majid, S. A., with Sinton, 816 (Mal.)
 Majumdar, A. R., 464 (B.R.)
 Malamos, B., 124, 125 *bis* (Mal.), 718 (S.S.)
 —, with Denecke, 423 (Mal.)
 — & Nauck, E. G., 797 (Mal.)
 —, with —, 800 (Mal.)
 Maldonado, A., (584) (Fev.)
 Maldonado Sampedro, M., (147) (Mal.), 639 (Hel.)
 Mallik, K. L. B., (655) (Hel.)
 Malowitschko, E. & Puppenko, I. G., (199) (Am.)
 Manai, A., 70 (Misc.)
 Manako, K., (772) *bis* (Chl.)
 Manalang, C., 865 (Lep.)
 Manca, S., 414 (Mal.)
 Manouélian, Y., 605, 618 (Rab.)
 Manson, D., 111, 135, 414 (Mal.), 235 (Hel.)
 Manson-Bahr, P., 407 (Mal.), (532), (915) (Misc.)
 —, with Low, 274 (Hel.)
 Manwell, R. D., 119, 796 (Mal.)
 Maplestone, P. A., 642 (Hel.)
 Marchal, G., Soulié, P. & Grigaut, A., (279) (Hel.)
 Marchoux, E., 329 (Lep.)
 — & Chorine, V., 546 (Lep.)
 Marin, R. A., with Levine, 627 (Hel.)
 Marinesco, G. & Draganesco, S., 179, 617 (Rab.)
 — & Façon, E., 617 (Rab.)
 Marini, C., with Villain & Dupoux, 805 (Mal.)
 Marino, A. W. M., (199) (Am.)
 Mariotti, E., with Ascione, 794 (Mal.)
 Markianos, J., with Lépine, 546 (Lep.)
 de Marqueissac, H., 695 (S.S.)
 Marsh, F., with McClean, 194 (Dys.)
 Martillotti, F., (655) (Hel.)
 Martin & Arnaud, 631 (Hel.)
 Martin, F., with Grayson & Clark, (532) (Misc.)
 Martin, L. A., with Blanc, 566 (Fev.)
 Martin, P. H., 138 (Mal.)
 Martindale, W. E., with Barnes, Metcalfe & Lentz, 179 (Rab.)
 Martínez-Báez, M., 649 (Hel.)
 Martini & Zotta, 101 (Mal.)
 Martini, E., 907 (Misc.)
 Marty, M., 18 (S.S.)
 Marzinovsky, E., 673 (Misc.)
 Marzinowsky, E., (445) (Mal.)
 Masayama, S., 571 (Fev.)
 Masciotra, A. A., (147) (Mal.)
 Mason, M., 78 (B.R.)
 Massari, P., with Montel & Le-van-Phung, 55 (Y. & S.)
 Massias, C., (7) (Bb.), 112, 113 *bis* (Mal.), (227), 524, 525, (915) (Misc.), 498 (C.Bu.)
 —, Bourgin, P. & Nguyen-van-Tan, 420 (Mal.)
 Masuzawa, T., with Ota & Sato, 871 (Lep.)
 Mathew, R. Y., 905 (Misc.)
 Mathieu, V., with Walker, 892 (Y. & S.)
 Mathis, C., 284 (Y.F.), (782) (Am.),
 —, Durieux, C. & Advier, M., 288 (Y.F.)
 —, Laigret, J. & Durieux, C., 284 (Y.F.)
 — & Mathis, M., 287 (Y.F.)
 Mathis, M., 292, (882) (Y.F.)
 —, with Nicolau & Kopciowska, 293 (Y.F.)
 Matsuda, S., 177, 609 (Rab.)
 Matsumoto, K., with Suzuki & Sugio, 376 (Sn.)
 Matsuo, S., with Hayashi, Kato & Okamoto 169 (Fev.)
 Matthes, H. C., 442 (Mal.)
 Mauro, M., (147) (Mal.)
 Maury, M., with Millous, 18 (S.S.)
 Maxwell, J. L., 860 (Lep.)
 Mayeozoko, S., 634 (Hel.)
 Mayer, M., 226 (Misc.), 481 (K.A.)
 Mazza, S., 37 *ter*, 38, (371), 717 (S.S.)
 — & Almaraz, P., 37 (S.S.)
 — & Guerrini, F. Z., 36 (S.S.)
 — & Jorg, M. E., (43) (S.S.)
 — & Miyara, J. S., 717 (S.S.)
 —, —, Basso, G. & Basso, R., 717 (S.S.)
 — & Romafa, C., (43) (S.S.)
 Mazzolani, C., (915) (Misc.)
 Measham, J. E. & Chowdhury, M. U., 804 (Mal.)
 Mededeelingen van den Dienst der Volksgezondheid in Nederlandsch-Indië, (227) (Misc.)
 Medulla, C., 561 (Fev.)
 Megaw, J., 153 (Fev.)
 Megaw, J. W. D., with Rogers, 151 (B.R.)
 Méhes, J., (7) (Bb.)
 — & Peter, F., (7) (Bb.)
 Mehta, D. R., 435, 808 (Mal.)
 Meighan, S. S., 895 (Oph.)
 — & Peter, F., (7) (Bb.)

- de Meillon, B., 133 (Mal.)
 Meira, J. A., with Pessôa, 839 (B.R.)
 Meloney, H. E., (199) (Am.)
 — & Crabtree, J. A., 107 (Mal.)
 — & Frye, W. W., 190, 779 (Am.)
 — & Harwood, P. D., 668 (Misc.)
 Melikowa, T. A., with Bogojawlenski & Demidowa, 482 (K.A.)
 Mellanby, K., 669 (Misc.)
 de Mello, F., 784 (Mal.)
 Memorskij, W., (894) (Y. & S.)
 Mendioroz, J., (348) (Lep.)
 Menon, T. B. & Annamalai, D. R., 273 (Hel.)
 —, Krishnaswamy, T. K. & Annamalai, D. R., 789 (Mal.)
 Mercier, H., with Sicé, 21, 349 (S.S.)
 Merken, G., 724 (S.S.)
 Merklen, P. & Israël, L., 492 (K.A.)
 Mertens, W. K., with Hoffmann & Snijders, 171 (Fev.)
 Mesnard, J. & Delbove, P., 157 (Fev.)
 — & Toumanoff, C., (753) (Mal.)
 Metcalfe, A. N., with Barnes, Martindale & Lentz, 179 (Rab.)
 Metelkin, A., 660 (Misc.)
 Mettam, R. W. M., with Duke & Wallace, 33 (S.S.)
 Meyer, F., (470) (Pel.)
 Mezger, J., with Roubaud, 121 (Mal.), 449 (Pl.)
 Miguelotte-Vianna, M., with Vellard, 380 (Sn.)
 Mihăilescu, M. & Nicoloff, D., 490 (K.A.)
 Milam, D. F., 167 *bis* (Fev.)
 Milasch, G. P., 552 (Lep.)
 Miller, D. K., with Rhoads, 48 (Sp.), 906 (Misc.)
 Miller, H. M., Jr., 634 *bis* (Hel.)
 — & Gardiner, M. L., 255 (Hel.)
 Miller, R., 45 (Sp.)
 Millischer, F., 775 (Am.)
 —, with Fillion, 658 (Misc.)
 Millous, M. & Maury, M., 18 (S.S.)
 Mills, S. R., 467 (Pel.)
 Milne, J. C., 96 (Mal.)
 Minamizaki, Y., 619 (Hel.)
 Minatoya, T., 212 (Bl.)
 Minec, with Grimes & Cluzet, 869 (Lep.)
 Minerwin, S. M., Stupnitzki, P. N. & Tinker, J. S., 455 (Pl.)
 Minett, F. C., 821 (Bl.)
 Mingazzini, U., (147) (Mal.)
 Mingelen, R., with Houwer, 898 (Oph.)
 Missiroli, A., 304 (B.R.), 795, 807 (Mal.)
 —, with Hackett, 809 *bis* (Mal.)
 — & Mosna, E., 794 (Mal.)
 Mitchell, E. C. & Goltman, D. W., (753) (Mal.)
 Mitra, B. N., 768 (Chl.)
 —, with Linton, 461 (Chl.)
 —, with — & Shrivastava, (462) (Chl.)
 Miyahara, H., with Morishita & Ishioka, 745 *bis* (Mal.)
 Miyara, J. S., with Mazza, 717 (S.S.)
 Miyara, S., with Mazza, Basso, G. & Basso, R., 717 (S.S.)
 Miyazawa, M., with Nishibe, 162 (Fev.)
 Moberg, E., (147) (Mal.)
 Moir, K. T., 207 (Bl.)
 Moiser, B., 545 (Lep.)
 Moldawska-Kritschewskaja, W. D. with Sinelnikow, Gorchowa, Althausen & Gritzay, 792 (Mal.)
 Molina, R. R., with Bachman & Gonzalez, 268 (Hel.)
 Mollaret, P. & Stefanopoulo, G. J., 292 (Y.F.)
 —, with —, 284 (Y.F.)
 —, with — & Desnos, 290 (Y.F.)
 Molloy, D. M., with Lamson & Brown, 635 (Hel.)
 de Monbreun, W. A., 219 (Misc.)
 Moncrieff, A., & Whitby, L. E. H., 72 *bis* (Misc.)
 Monier, H. M., Guy, R. & Ros, M., 401 (Mal.)
 —, with Saleun, 741 (Mal.)
 Monnerot-Dumaine, (820) (Mal.)
 Monnier, E., with Morin, Bader & Moreau, 727 (Mal.)
 Monserrat, C., 547 (Lep.)
 Montañés, P., 855 (Lep.)
 — & Negro, E., (92) (K.A.)
 Monteiro, J. L., 159, 580 *bis*, 581, 582 (Fev.)
 —, with Travassos, 581 (Fev.)
 Montel, L., (279) (Hel.)
 Montel, L. R., 344, 345 *bis*, 346 (Lep.)
 Montel, M., 649 (Hel.)
 Montel, M. L. R., 545, (555), 547 (Lep.)
 —, Massari, P. & Le-van-Phung, 55 (Y. & S.)
 — & Nguyen-Ngoc-Nhuan, (555) (Lep.)
 — & Truong-van-Que, 346, 549 (Lep.)
 Montel, R. & Truong-van-Que, (555) (Lep.)
 Montestruc, E., 340 (Lep.), 892 (Y. & S.)
 Montpellier, J. & Catanei, A., 182 (Der.)
 Montschadsky, A., 908 (Misc.)
 de Moor, C. E., with Lampe, 863 (Lep.)
 Moore, M., 218 (Misc.)
 Moorthy, V. N., 654 (Hel.)
 Morales-Otero, P. & Pomales-Lebrón, A., 74 (Misc.)
 Moreau, P., (445) (Mal.)
 —, with Morin, Bader & Monnier, 727 (Mal.)
 —, with Sicé, 547 (Lep.)
 Moreira, J. A. & de Magalhães, O., 157 (Fev.)
 Morgan, M. T., 585, (882), (Y.F.)
 Morin, H. G. S., 430, (753) (Mal.)
 —, Bader, H., Monnier, E. & Moreau, P., 727 (Mal.)
 — & Carton, P., (753), (820) (Mal.)
 Morishita, K., (753) (Mal.)
 —, Miyahara, H. & Ishioka, H., 745 *bis* (Mal.)
 Morison, J., 764 (Chl.)
 —, Rice, E. M. & Haythornthwaite, R. A., 460 (Chl.)
 Moroder, J., (43) (S.S.)
 Morris, K. R. S., 40 (S.S.)
 Moshkovsky, S. & Burova, L., 409 (Mal.)
 — & Poliakov, A., 409 (Mal.)
 Mosna, E., 432 (Mal.)
 — with Missiroli, 794 (Mal.)
 Mostajo, B., with Long, 448 (Pl.)
 Mostert, H. v. R., 859 (Lep.)
 Mouchet, R., van Hoof, L., Duren, A., Fornara, L., Clarebout, G., Henry, E. & Henrard, C., 280 (Y.F.)

- Moursund, W. H., with Kemp & Wright, 296 (R.F.)
 Mourzinn, A. N. & Souchkova, E. G., 473 (Oph.)
 Moutoussis, K., 337 (Lep.)
 Mu, J., 636 (Hel.)
 Mueller, J. F., (655) (Hel.)
 Muench, H., with Boyd & Stratman-Thomas, 405 (Mal.)
 —, with Howard & Earle, 739 (Mal.)
 Mühlens, P., 109, 406, (753) (Mal.), 515 (Misc.), (782) (Am.)
 Muir, E., 341, 542 (Lep.)
 — & Chatterji, K. R., 539, 543 (Lep.)
 Mukerji, S., with Smith & Krishnan, 88 (K.A.)
 Mukherjee, S. N., with Chopra & Sen, 789 (Mal.)
 Mulligan, H. W., 797 (Mal.)
 —, with Sinton, 122 (Mal.)
 Mulrennan, J. A., with Boyd, 135 (Mal.)
 —, with — & Cain, 806 (Mal.)
 Muñoz Ochoa, M., with Strong, Sandground & Bequaert, 300 (B.R.)
 Murashima, T., 195 (Dys.)
 Muratowa, A. P., 173 (Rab.)
 Murgatroyd, F., with Lourie & Yorke, 697 (S.S.)
 —, Russell, H. & Yorke, W., 26 (S.S.)
 —, with Yorke, 518 (Misc.)
 Murphy, R. A., 141, 412 (Mal.)
 Murray, A. J., 826 (Bl.)
- N**
- Nabokich, P., with Beklemischew, Schipizina & Polowodowa, 907 (Misc.)
 Nadler, J. E., Green, H., & Rosenbaum, A., 216 (Misc.)
 Nagayoshi, Y., with Kawai & Koo, 187 (Am.)
 Nägelsbach, E., 207 (Bl.), (445) (Mal.) (894) (Y. & S.)
 Nakamura, K. & Kobashi, S., 339 (Lep.)
 Nakamura, T., 378 (Sn.)
 Narayana Rao, Y. S., 764 (Chl.)
 Narihara, N., 254 *bis* (Hel.)
 Nash, T. A. M., 39, 723 *bis* (S.S.)
 Nath, M. C., with Ghosh, 422 (Mal.)
 Nattan-Larrier, L., 43 (S.S.)
 — & Grimard, L., 485 (K.A.)
 — & Grimard-Richard, L., 85 *ter*, 87, 484 (K.A.)
 —, — & Nougues, S., 85 (K.A.)
 —, Nougues, S. & Grimard-Richard, L., 85 (K.A.)
 Nauck, E. G., 116 (Mal.)
 —, with Hegler, 77 (B.R.)
 — & Malamos, B., 800 (Mal.)
 —, with —, 797 (Mal.)
 Naumann, H. E., 200 *bis* (Bl.)
 Nayar, K. K., with Wright & Nayudu, 476 (Oph.)
 Nayudu, T. V., with Wright & Nayar, 476 (Oph.)
 Nechkovitch, M., 381 (Sn.)
 Negro, E., with Montañés, (92) (K.A.)
 Negroni, P., 185 (Der.)
 Neitz, W. O. & Thomas, A. D., 616 (Rab.)
- Nelson, E. C., 225 (Misc.)
 d'Netto, S. G., with Vickers & West, 139 (Mal.)
 Neuber, E., 648, 649 (Hel.)
 Neumann, H., with Schilling, Schreck & Kunert, 43 *bis* (S.S.)
 Newman, C. D. & Chalam, B. S., 417 (Mal.)
 Ngo-Quang-Ly, with Dorolle, 545, (554) (Lep.)
 —, with — & Tran-Van-Tam, 346 (Lep.)
 Nguyen-van-Lien, with Guillermin & Banos, 342 (Lep.)
 Nguyen-Ngoc-Nhuan, with Montel, 555 (Lep.)
 Nguyen-van-Tan, with Massias & Bourgin, 420 (Mal.)
 Nicholls, L., 763 (Chl.)
 Nicol, W. D., with James & Shute, 737 (Mal.)
 Nicolas, C., 546 (Lep.)
 Nicolau, S. & Kopciowska, L., 173, 605 (Rab.)
 —, — & Mathis, M., 293 (Y.F.)
 —, with Slatineanu & Balmus, 741 (Mal.)
 Nicolle, C., 284 (Y.F.), 560 (Fev.), 589 (Y.F.)
 — & Giroud, P., 557, 558 *bis*, 559, (582) (Fev.)
 — & Laigret, J., 880 (Y.F.)
 — & Sparrow, H., 158, 560, 578 (Fev.)
 Nicoloff, D., with Mihăilescu, 490 (K.A.)
 Nieschulz, O. & du Toit, R. M., 663 (Misc.)
 Nigg, C., 569 (Fev.)
 Nijkamp, J. A. & Swellengrebel, N.H., 136 (Mal.)
 Ninni, C. & Tramontano, V., 486 (K.A.)
 Niño, F. L., 184 (Der.), (227) (Misc.), 269 (Hel.)
 — & Triaca, J. A., (227), (674) (Misc.)
 Nishibe, M. & Miyazawa, M., 162 (Fev.)
 van Nitsen, R., 100, 408, 742 (Mal.), 248 (Hel.)
 — & Duwez, J., 306 (B.R.)
 Nittis, S., (873) (Lep.)
 Nitzulescu, J., with Slatineanu, Balteanu, Sibi, Franche, Catacuzino, Paraschivescu, Veit & Lupu, 469 (Pel.)
 Nolasco, J. O., 343, 344, 535 (Lep.)
 Noosten, H. H., Kirschner, L. & Vos, J. J. T., 73 (Misc.)
 Noronha, A. J., 254 (Hel.)
 Noshokati, H., with Azmy & Gaafar, 527 *bis* (Misc.)
 Nossina, V., 776 (Am.)
 Nougues, S., with Nattan-Larrier & Grimard-Richard, 85 (K.A.)
 Noury, M., with Blanc, Baltazard, Bruneau & Barneoud, 163 (Fev.)
 Novák, E., with von Janssó, 596 (R.F.)
 Novet, D., Benoît, G. & Atmann, R., (820) (Mal.)
 Nursing, D., Rao, B. A. & Sweet, W. C., 399 (Mal.)
 Nykamp, J. A., with Swellengrebel, 136 (Mal.)
- O**
- Occhino, A. & Kernkamp, Y., 56 (Y. & S.)
 O'Connor, F. W., (532) (Misc.)
 O'Connor, M. P., 577 (Fev.)

- d'Oelsnitz, Bonnet, G. & Raybaut, A., 493 (K.A.)
 —, Galavielle, R. & Raybaut, A., (493) (K.A.)
 — & Ronchèse, A. D., 86 (K.A.)
 Oesterlin, M., 250 *bis* (Hel.)
 — & Krainick, H., 236 (Hel.)
 Office International d'Hygiène Publique, Paris, 459 (Chl.)
 O'Flynn, J. A., (470) (Pel.)
 Ogiuti, K., with Tani, 57 (Y. & S.)
 O'Hara, J. A., (147) (Mal.)
 Ohira, T., (655) (Hel.)
 Ohmori, N., 670, 913 (Misc.)
 Ohtawara, T., 864 (Lep.)
 Ohtsuka, I., with Ozaki, 563 (Fev.)
 Okamoto, N., with Hayashi, Matsuoka & Kato, 169 (Fev.)
 Okamoto, Y., with Kasahara & Yoshida, 566 (Fev.)
 Okounovski, J. & Khakhaieva, V., 662 (Misc.)
 Olavarria, J. & Hill, R. B., 815 (Mal.)
 —, with —, (147) *bis* (Mal.)
 —, with — & Rivera, 814 (Mal.)
 de Oliviera Castro, G. M. & Bier, O., (583) (Fev.)
 Oliver, J., with Bachman, 268 (Hel.)
 Oliver, W. W., (199) (Am.)
 Orenstein, A. J., 235 (Hel.)
 Ota, M. & Ishibashi, T., 551 (Lep.)
 — & Sato, S., 338 (Lep.)
 —, —, Sato, S. & Ishibashi, T., (555) (Lep.)
 —, — & Masuzawa, T., 871 (Lep.)
 Oteiza y Setién, A. & Tiant y del Río, F. R., 855 (Lep.)
 Othaz, E. L., 185 (Der.)
 Otto, I. H., & Tschan Tsching Ji, 630 (Hel.)
 Otto, J. H., (655) (Hel.)
 Otto, R., 153 (Fev.)
 Owen, W. B., Honess, R. F. & Simon, J. R., 188 (Am.)
 Oxenius, K., (655) (Hel.)
 Ozaki, Y. & Ohtsuka, I., 563 (Fev.)

P

- Packchianian, A., 35, 711 (S.S.)
 Padovani, S., 897 (Oph.)
 Paget, H., Trevan, J. W. & Attwood, A. M. P., 343 (Lep.)
 Pagonis, A., with Caminopetros, Contos & Pheloukis, 575 (Fev.)
 Paic, M., with Levaditi & Vaisman, 298 (R.F.)
 Palais, M., 253 (Hel.)
 Palawandow, H., Serebrennaja, A. I. & Pugatsch, E. M., 609 (Rab.)
 Paldrock, A., 347, 871 (Lep.)
 — & Pooman, A., 340 (Lep.)
 Palit, A. N., (915) (Misc.)
 Pallary, P., 227, 243 (Hel.)
 Palmer, F. J., 73, (227) (Misc.)
 Pampana, E. J., 410 (Mal.)
 Pan, C., 476 (Oph.)
 Panayotatou, A., (583) (Fev.)
 Pandalai, N. G., 599 (R.B.F.)
 Pandit, C. G., 841 (Pl.)
 Paolo, R., (445) (Mal.)
 Papazian, R., with Vasilescu, (782) (Am.)
 Paradiso, F. & Fiorentino, A., 534 (B.R.)
 Paras, A., with Lagrosa, Alonso & Tiong, 547 (Lep.)
 Paraschivescu, Z., with Slatineanu, Balteanu, Sibi, Nitzulescu, Franche, Cantacuzino, Veit & Lupu, 469 (Pel.)
 Pardina, J. M., 230 (Hel.), 904 (Misc.)
 Paretskaya, M., with Yatsenko & Kipritch, 666 (Misc.)
 Paris Eguilaz, H., (43) (S.S.)
 Parker, R. R., 517 (Misc.)
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